EXHIBIT DX1

TO DECLARATION OF BENJAMIN W. HULSE IN SUPPORT OF DEFENDANTS' MOTION FOR RECONSIDERATION OF THE COURT'S DECEMBER 13, 2017 ORDER ON GENERAL CAUSATION

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■ ARTHROPLASTY

Forced-air warming and ultra-clean ventilation do not mix

AN INVESTIGATION OF THEATRE VENTILATION, PATIENT WARMING AND JOINT REPLACEMENT INFECTION IN ORTHOPAEDICS

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We investigated the capacity of patient warming devices to disrupt the ultra-clean airflow system. We compared the effects of two patient warming technologies, forced-air and conductive fabric, on operating theatre ventilation during simulated hip replacement and lumbar spinal procedures using a mannequin as a patient. Infection data were reviewed to determine whether joint infection rates were associated with the type of patient warming device that was used.

Neutral-buoyancy detergent bubbles were released adjacent to the mannequin's head and at floor level to assess the movement of non-sterile air into the clean airflow over the surgical site. During simulated hip replacement, bubble counts over the surgical site were greater for forced-air than for conductive fabric warming when the anaesthesia/surgery drape was laid down ($p = 0.010$) and at half-height ($p < 0.001$). For lumbar surgery, forced-air warming generated convection currents that mobilised floor air into the surgical site area. Conductive fabric warming had no such effect.

A significant increase in deep joint infection, as demonstrated by an elevated infection odds ratio (3.8, $p = 0.024$), was identified during a period when forced-air warming was used compared to a period when conductive fabric warming was used. Air-free warming is, therefore, recommended over forced-air warming for orthopaedic procedures.

It has been acknowledged that the operating theatre's ventilation system has a critical role in preventing joint infection.[1] Charnley postulated that the 'surgical implant might provide a nidus for the growth of airborne bacteria which ordinarily are accepted as non-pathogenic'.[1] This has been confirmed through animal studies[2] and a national clinical trial involving over 8000 operations demonstrating the contribution of clean air to the reduction of the rate of infection after arthroplasty.[3] Following that report, ultra-clean ventilation became the standard for joint replacement procedures. The system protects the surgical site from airborne contamination through the constant delivery of a downward uniform-velocity (0.3 m/s to 0.5 m/s), highly filtered (> 99.997%) airflow.[4] However, the performance of ultra-clean ventilation depends critically on airflow volumes and proper temperature gradients. The latter may be disrupted by excess heat released by patient warming devices.

Forced-air warming is now commonly used in operating theatres to ensure normothermia of the patient. The vented airflow from forced-air warming is released at up to 43°C, which is often 20°C above ambient operating theatre conditions.[5,6] The release of excess thermal energy can establish temperature gradients that impede the downward flow of ultra-clean air. Reductions in the velocity of downward flow have also been shown to increase the entry of contaminants into the surgical site.[7] In addition, the release of heat may generate convection currents that rise against the downward airflows, drawing non-sterile floor-level air into the surgical site.

Air-free alternatives, such as conductive fabric warming, have been developed that are comparably effective for the prevention of hypothermia.[8-14] These offer higher thermal efficiencies than forced-air warming and therefore release only a fraction of the excess heat.[6] Accordingly, we chose to compare the effects of forced-air and conductive fabric warming on clean airflow patterns over the surgical site in a partial-walled ultra-clean operating theatre during two simulated procedures: a hip replacement with upper-body warming, and a lumbar spinal procedure with lower-body warming. Ventilation airflow patterns were

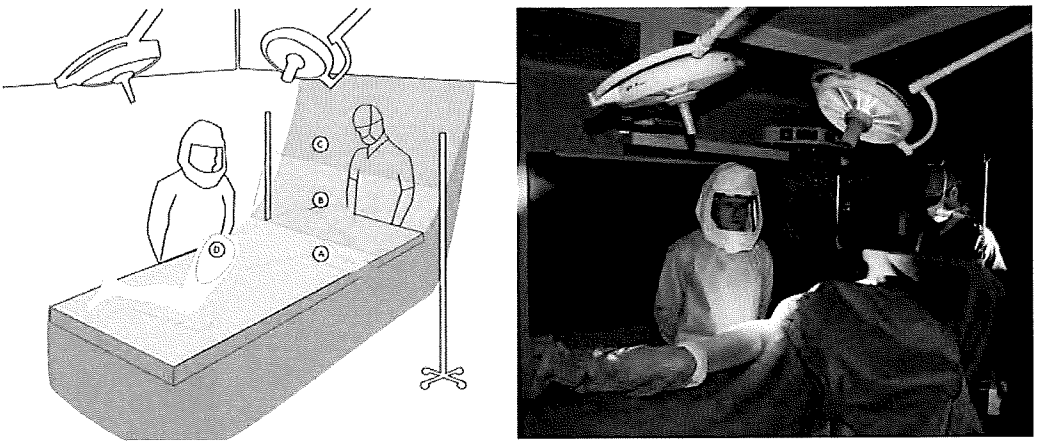

Fig. 1

Diagram (left) and photograph (right) showing the operating theatre set-up for hip replacement with upper-body warming showing surgical drape positions of laid-down (A), half-drape (B) and full-drape (C) and surgical site location (D).

visualised using neutrally buoyant detergent bubbles. In addition, observational data on arthroplasty infection rates were compared for the period each warming device was in clinical use in our hospital.

Materials and Methods

Ultra-clean operating theatre characteristics. Experiments were carried out in a partial-walled ultra-clean operating theatre (ExFlow 90; Howorth, Bolton, United Kingdom) used for orthopaedic and spinal surgery in the United Kingdom. Validation and verification checks according to Hospital Technical Memorandum 2025[15] showed the operating theatre airflows to be within specification and having a mean velocity of 0.44 m/s at a height of 2 m, which exceeds the threshold required by the standard (0.38 m/s). Owing to the location of the theatre preparation room an insignificant airflow imbalance was detected that affected the results of a single-particle entrainment test: entrainment values were 12% at that location, which marginally exceeded the recommended threshold of 10%.

Airflow visualisation procedures. High-intensity lighting was used to illuminate neutrally buoyant detergent bubbles having a diameter of approximately 4 mm (referred to here as 'bubbles'). A SAI bubble generator (SAI Model 5; Sage Action Inc., Ithaca, New York) was used to produce bubbles using a helium-mixed air supply and detergent. The equipment uses a centrifugal classifier to allow only bubbles of neutral buoyancy through the system, with heavier or lighter bubbles discarded. The bubble generator is specifically designed and validated for the visualization of air currents.[16] For photography, a digital camera (EOS 500D; Canon, Reigate, United Kingdom) was used and exposure time set to 0.25 s for time-lapse photography.

Experimental setup. ***Hip replacement.*** A mannequin was laid in the lateral position on an operating table and draped with a three-piece disposable draping set (Molnlycke Health Care, Manchester, United Kingdom) in accordance with standard protocols (Fig. 1). The drapes had adhesive edges and all were sealed during draping. A surgeon, dressed in occlusive clothing with head gear (T4; Stryker, Kalamazoo, Michigan), stood motionless in front of the surgical site and an anaesthetist stood at the head of the operating table. At the head end the drape was used to create an anaesthesia screen in one of three positions, either clipped to the ceiling to create a barrier between the surgical site and the anaesthesia area (full-drape); clipped to the intravenous stands and raised 0.75 m above the operating table (half-drape); or laid down over the mannequin's head (laid-down). The upper-body warming treatment was introduced under the drape and was either a torso forced-air blanket (Bair Hugger Model 540; Arizant Healthcare, Eden Prairie, Minnesota) or a torso conductive fabric blanket (Hot Dog Model B110; Augustine Temperature Management, Eden Prairie, Minnesota). The warming devices were powered by standard controllers set to 43°C. Bubbles were introduced at the head/neck of the mannequin to track under-drape resident air movements in the region where the excess heat from patient warming was being released.

Lumbar spinal procedure. The same mannequin was laid in the prone position on the operating table and four drapes were arranged in a square configuration (Molnlycke Health Care) with the screen at full height (Fig. 2). A single surgeon stood motionless next to the surgical site for all experiments. A standard theatre gown and face mask were worn by the surgeon. The lower-body warming treatment was introduced under the drape and was either a lower-body forced-air blanket (Bair Hugger Model 525; Arizant

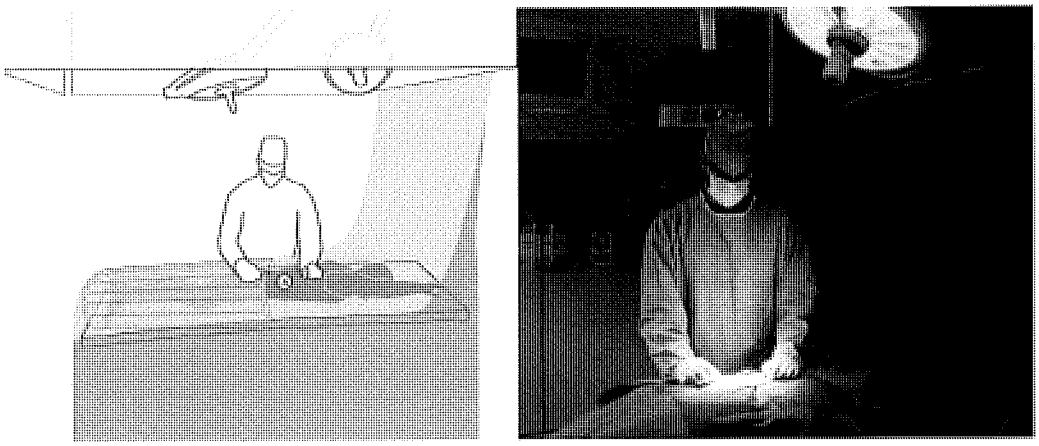

Fig. 2

Diagram (left) and photograph (right) showing the operating theatre set-up for lumbar spinal surgery with lower-body warming and full-drape, showing surgical site location (A).

Fig.3a

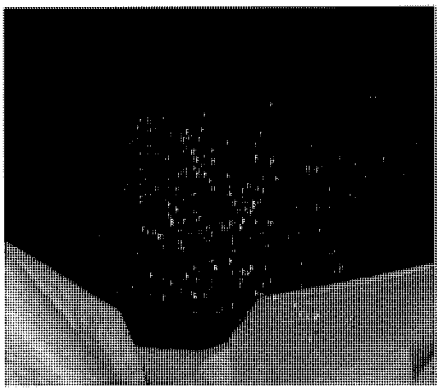

Fig.3b

Photographs showing a) the definition of the region where bubble counts were performed over the surgical site for hip replacement with upper-body warming, with bubbles (white steaks) appearing in the photograph for the experimental setup of forced-air warming and half-drape, and b) bubbles exiting the diffuser in still air.

Healthcare) or a lower-body conductive fabric blanket (Hot Dog Model B103; Augustine Temperature Management). The deviceswere powered by the same controllers as listed above and set to 43°C. Bubbles were introduced at floor level between the surgeon's body and the operating table in the area where the excess heat from patient warming was being released.

Sampling procedures. ***Hip replacement.*** Bubble counts over the surgical site were measured using a sequence of five photographs taken at ten-second intervals. The number of bubbles reaching the surgical site was determined by counting the number of bubbles in a 0.5 × 0.5 m region over the surgical site in each photograph (Fig. 3).

Lumbar spinal procedure. A different airflow pattern was observed with the spinal simulation, therefore time-lapse photography was chosen rather than bubble counts for data presentation. Time-lapse photography also provides directional information on airflow patterns that cannot be easily captured in quantitative data.

Experimental design. ***Hip replacement.*** . A replicated (n = 2) $3^1 2^1$ full factorial design was used to assess changes in bubble counts over the surgical site. The experimental factors considered were the anaesthesia/surgery screen: laid-down, half-screen or full-screen; and the patient warming device: conductive fabric or forced-air.

Lumbar spinal procedure. . No design was either used or necessary to demonstrate the difference in ventilation performance between forced-air and conductive fabric warming systems.

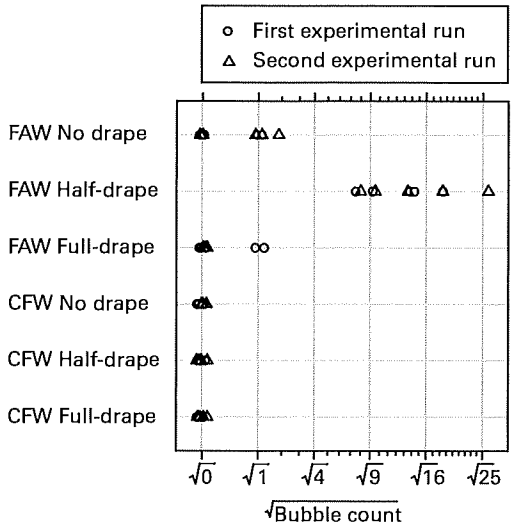

Fig. 4

Chart showing bubble counts over the surgical site for each photograph (data are staggered for clarity). Five photographs were taken for each experimental run (FAW, forced-air warming; CFW, conductive fabric warming).

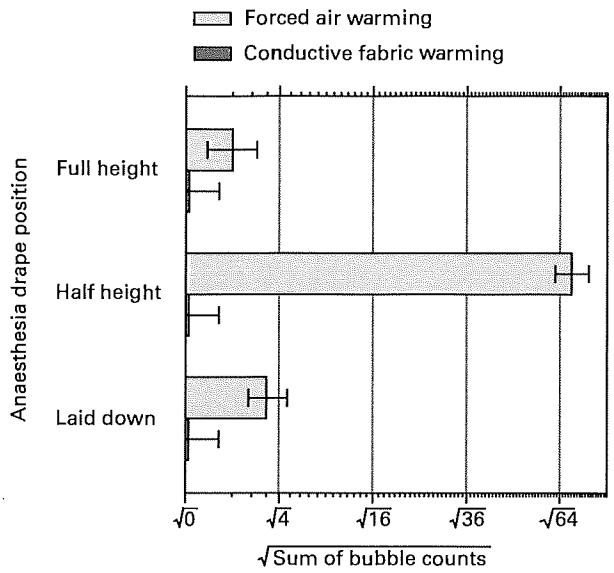

Fig. 5

Bar chart showing the mean bubble count for experimental runs when the bubble counts were summated over the five photographs. Error bars represent the standard error of the mean. Wald tests were used for statistical inference.

Joint infection data. Demographic information on relevant risk factors for surgical site infection (SSI) were collected for primary hip and knee replacement procedures performed at our hospital during a 2.5-year period starting 1 July 2008. Infection was diagnosed by SSI nurses according to English Health Protection Agency criteria for deep infection.[17] In order to standardise the duration of follow-up, only infections presenting within 60 days of surgery were included. Microorganism identification was performed on isolates from septic joints. A transition in patient warming systems from forced-air to conductive fabric was made in all three elective orthopaedic theatres, starting on 1 March 2010 and ending on 1 June 2010. Unfortunately, the prophylactic antibiotic regimen was not constant during the study period. From July 2008 to February 2009, a single dose of gentamicin 4.5 mg/kg was given at induction. In March 2009 this was changed to teicoplanin 400 mg and gentamicin 3 mg/kg. Gentamicin-loaded cement (0.5 g per 40 g mix) was used for both groups. Similarly, the thromboprophylaxis regimen from July 2008 to the end of July 2009 was tinzaparin (Leo Pharma, Princes Risborough, United Kingdom) from day one to day 14 or 28 post-operatively for knee or hip replacement, respectively. From August 2009 to February 2010 rivaroxaban (Bayer PLC, Newbury, United Kingdom) was provided from day one post-operatively, but in February 2010 to the end of the study this reverted to tinzaparin from day one post-operatively.

Statistical analysis. A Poisson regression model was fitted to the hip replacement data having the sum of bubble counts for each experimental run (five photographs) as the response and the factors identified in the experimental design as predictors. Differences in demographics and comorbidities between the patient warming groups were assessed by analysis of variance (ANOVA) or log-linear contingency table methods. Univariate odds ratios (OR) for the development of joint sepsis were computed using separate logistic regression models for each risk factor. Logistic regression was used to determine mean infection rates and dispersion indices for the periods of forced-air warming, transition and conductive fabric warming. Further details on statistical methods are provided in each table or figure. A p-value < 0.05 was considered statistically significant.

Results

Hip replacement. Bubble counts per photograph show that forced-air warming mobilised under-drape air so that it passed over the anaesthesia/surgery drape and into the surgical site (Fig. 4), but conductive fabric warming did not have a mobilising effect. Further, the position of the drape had a large effect on under-drape air mobilisation for forced-air warming.

Based upon Wald tests, differences in the sum of bubble counts for each experimental run (Fig. 5) were significant between conductive fabric and forced-air warming for the drape configurations of half-drape (0 *versus* 68, $p < 0.001$) and laid-down (0 *versus* 3, $p = 0.010$); differences for full-drape (0 *versus* 1, $p = 0.283$) did not reach statistical significance.

Lumbar spinal procedure. Excess heat from forced-air warming resulted in the development of hot-air convection currents between the surgeon's body and the operating table that transported floor-level air upwards and into the surgical

Table I. Demographics of surgical site infection risk factors by patient warming device (SEM, standard error of the mean)

	Forced-air warming	Conductive fabric warming	p-value*
Mean age (years) (SEM)	68.7 (0.30)	68.8 (0.50)	0.867†
Number of procedures (n)			
Hip	423	135	-
Knee	643	236	-
Hip : knee (%)	*40:60*	*37:63*	0.261
Diabetes (n, %)			
Type I	17 (*1.6*)	6 (*1.6*)	0.976
Type II	127 (*11.9*)	36 (*9.7*)	0.240
Duration of pre-operative hospital stay (n)			
0 days	990	357	
≥ 1 days	76	17	
0 : ≥ 1 (%)	*93:7*	*95:5*	0.075

* likelihood ratio chi-squared test (contingency table), unless otherwise stated
† analysis of variance

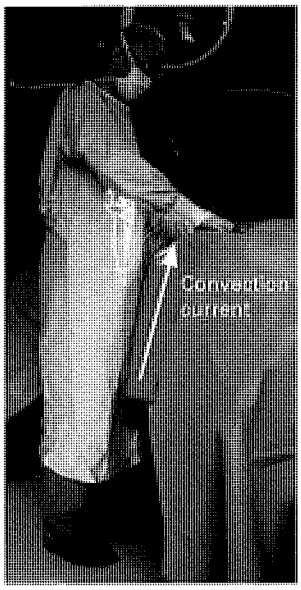

Fig. 6a

Fig. 6b

Time-lapse photographs of bubbles depicting airflow patterns for a lower lumbar spinal implant procedure with a) forced-air warming with the resulting convection current annotated, and b) with conductive fabric warming.

site (Fig. 6). In contrast, conductive fabric did not release sufficient excess heat to establish these convection currents.

Joint infection risks. The demographics of 1437 patients undergoing hip or knee replacement revealed no significant difference between the two types of warming for SSI risk factors of age, type of surgery, diabetes and length of pre-operative stay (Table I). Unfortunately, record keeping was incomplete for the additional risk factors of blood transfusion, obesity, incontinence and fitness for surgery, which have been identified elsewhere as important predictors for deep infection.[4,18]

The risks of developing deep infection (Table II) were significantly greater for patients undergoing hip *versus* knee replacement (OR 4.1, $p < 0.001$), and patients treated with forced-air *versus* conductive fabric warming (OR 3.8, $p = 0.024$). The factors of age, diabetes and pre-operative length of stay had no significant impact on the risk of infection. Further, the ORs for hip *versus* knee infection were similar for the subgroups of forced-air and conductive fabric warming, having values of 4.1 and 3.5, respectively.

Micro-organisms isolated from septic joints were predominately skin commensals for both forced-air (81%) and conductive fabric (100%) warming (Table III); the remainder were from intestinal bacteria. Of the skin-based organisms, staphylococcus species were the most common sources of infection (93%).

Logistic regression identified a significant reduction in infection rates (Fig. 7) for the conductive fabric (0.8%) *versus* forced-air warming (3.1%) periods ($p = 0.024$, Wald test). Differences in infection rates were significantly different between the conductive fabric and transition periods (0.8% *versus* 3.7%, $p = 0.028$, Wald test); differences were not significant between the forced-air and transition periods (3.1% *versus* 3.7%, $p = 0.662$, Wald test).

Discussion

Forced-air warming was found to have a significant and disruptive impact on the clean airflow patterns over the surgical site compared to conductive fabric warming, which had no noticeable effect. Further, forced-air warming established convection currents that mobilised resident air from non-sterile areas such as the floor and under the anaesthesia/surgery drape into the surgical site. This disruption in the ventilation of the surgical site was associated with significantly higher risks of joint sepsis for the forced-air *versus* the conductive fabric warming groups.

Perhaps the most striking finding was the detection of hot-air convection currents originating where the 'mass flow' of hot air exited from the forced-air warming blanket:

Table II. Univariate comparison of risk factors on the development of deep joint infection (CI, confidence interval)

	Developing infection	Not developing infection	Odds ratio (95% CI)	p-value*
Age group (n, %)				0.818
Youngest third (≤ 64 years)	13 (*2.7*)	472 (*97.3*)	1.0	
Middle third (> 64 and < 73 years)	12 (*2.5*)	459 (*97.5*)	0.9 (0.4 to 2.1)	
Oldest third (≥ 73 years)	10 (*2.1*)	471 (*97.9*)	0.8 (0.3 to 1.8)	
Type of surgery (n, %)				< 0.001
Knee	10 (*1.1*)	869 (*98.9*)	1.0	
Hip	25 (*4.5*)	533 (*95.5*)	4.1 (1.9 to 8.6)	
Diabetes (n, %)				0.110
None	34 (*2.7*)	1219 (*97.3*)	1.0	
Type I or II	1 (*0.5*)	183 (*99.5*)	0.2 (0.0 to 1.4)	
Pre-operative stay (n, %)				0.327
0 days	34 (*2.5*)	1310 (*97.5*)	1.0	
1 or more days	1 (*1.1*)	92 (*98.9*)	0.4 (0.1 to 3.1)	
Patient warming device (n, %)				0.024
Conductive fabric	3 (*0.8*)	368 (*99.2*)	1.0	
Knee	1	235		
Hip	2	133		
Forced-air	32 (*3.0*)	1034 (*97.0*)	3.8 (1.2 to 12.5)	
Knee	9	634		
Hip	23	400		

* likelihood ratio chi-squared test (logistic regression)

Table III. Bacterial species isolated from septic hip and knees by patient warming device

	Forced-air warming	Conductive fabric warming
Number of operations	1066	371
Number of species identified		
Skin-carried		
Staphylococcus aureus	11	0
Staphylococcus aureus and CNS*	2	0
CNS	12	2
Other	1	1
Total	26	3
Intestinal		
Gram-negative bacteria	6	0
Total	6	0
Total	32	3

* CNS, coagulase-negative staphylococcus

for the hip replacement with upper-body warming convection currents formed near the mannequin's head, whereas for the spinal procedure with lower-body warming, convection currents formed along the lower drape edge by the surgeon's legs. The formation of such convection currents may at first appear to be theoretically unsupported, as forced-air warming exhausts a heated airflow of only 40 cubic feet per minute into a ventilation environment having an airflow of 6000 cubic feet per minute.[19] However, one must consider the effects of surgical lighting, drapes and personnel on ventilation, all of which create localized disturbances of airflow that aid the formation of convection currents.

Prior research in ultra-clean ventilation theatres has shown surgical lighting to be a significant source of disruption of ventilation through the downstream wake and associated recirculation zone.[20] In our study, the use of bubbles allowed us to visualise this recirculation zone, which was found to extend about 1 m below the body of each surgical light. The presence of a raised anaesthesia/surgery drape was shown to further magnify the size and effect of this vortex, as the drape blocked the natural passage of air out of the ventilation field and created a still zone. Lastly, the presence of a surgeon or anaesthetist near this zone created an added obstacle,[20] resulting in a situation where even the slightest movement adversely affected the natural airflow patterns over the surgical site. Under such fragile conditions the mass flow of hot forced-air being exhausted from the device was sufficiently buoyant to push upwards and into this locally compromised ventilation region.

The clinical concern regarding the formation of such convection currents is twofold. First, these currents oppose the natural clean airflow patterns that are intended to sweep contaminants down and away from the surgical site.[21] Thus, contaminants released in the vicinity of the surgical site are less likely to be cleared. Secondly, the upward mobilisation of floor-level and under-drape air could potentially compromise the sterility of the surgical site, as resident air from these locations is typically laden with pathogens shed from the surgical staff.[22] Either mechanism offers a plausible explanation for the significant association between the patient warming device and the risks of SSI in this study. Further, the types of organism isolated from septic joints were predominately skin flora and hence likely to have been transmitted by and deposited from the air.[23] It was, however, somewhat unusual that the odds of infection associated with hip replacement were

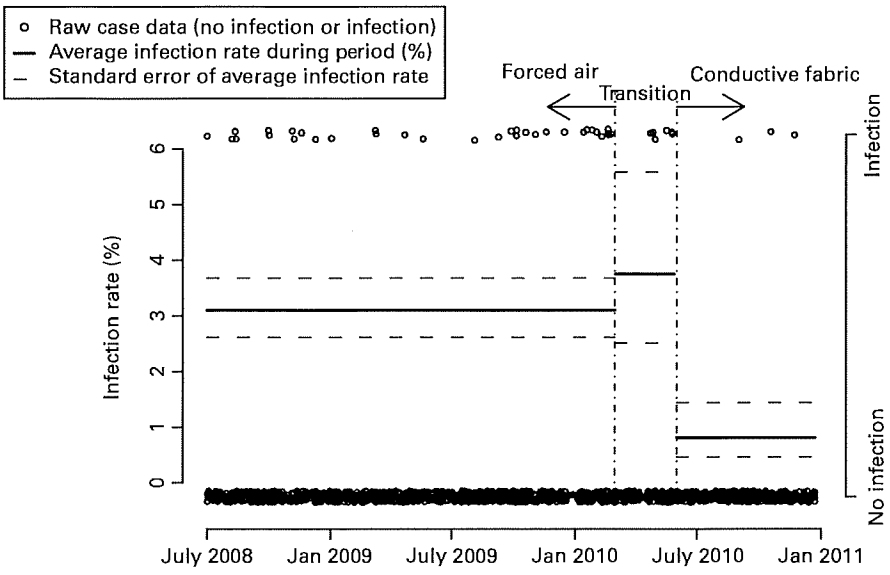

Fig. 7

Graph showing time-based trends of joint sepsis rates for hip and knee replacement cases. The outcome of each individual case is plotted on the right-hand axis (data are jittered to avoid overprinting). The infection rates for each period (forced-air, transition or conductive fabric) are plotted on the left-hand axis. Standard error of the mean was estimated using logistic regression.

4.1 times greater than the odds for knee replacement: typically, infection risks are greater for knee replacement.[24] A check of surgical practices revealed no differences in theatre dress or draping techniques between the procedures. Further, the OR for infection was consistent for both the forced-air and the conductive fabric subgroups (3.5 and 4.1, respectively), which suggests that there were no apparent changes in risk factors apart from warming device.

This study does not establish a causal basis for this association. Although the demographics were similar between the patient groups in terms of risk factors for infection, the data are observational and may be confounded by other infection control measures instituted by the hospital. For example, changes were made to the antibiotic and thromboprophylaxis protocols used during the study, although no infection control changes were made after February 2010.[25] In addition, we were unable to consider all factors that have been associated with SSI, as the details of blood transfusion, obesity, incontinence and fitness for surgery, which have been identified elsewhere as important predictors for deep infection,[4,18] were not sufficiently detailed in the medical record. Moreover, prior research is limited to a handful of studies that have either looked at the disruption in ventilation due to forced-air warming in conventional operating theatres[26,27] or evaluated accumulation microbial contamination and emission issues.[28-32] Research in ultra-clean operating theatres is limited to a single orthopaedic study in which forced-air warming resulted in elevated microbial counts over the surgical site.[33] However, the increase in contamination was deemed to be less than that resulting from the movement of personnel, and did not exceed recommended bacterial levels. It is not known how these results translate to the range of arthroplasty procedures performed in ultra-clean operating theatres. Even minor differences in factors such as draping, procedural practices and theatre dress are likely to have large effects on both floor-level and under-drape contaminant levels and the formation of convection currents.

National studies on the benefits of ultra-clean laminar-flow ventilation may provide a better indication as to the impact of forced-air warming on the mobilisation of contaminants, as they take into account the full range of surgical draping, procedural practices and theatre dress. Over the past ten years these studies have shown either an upwards trend towards[34] or significantly higher[24,35] infection rates in laminar flow. Yet the results of these studies are not fully conclusive, as they are limited by their clinical design, which omits basic air pollution endpoint measurements such as wound washout or slit sampling. Moreover, the mobilisation of non-sterile air due to forced-air warming may be the explanatory factor, as historical studies[1,3] on laminar-flow ventilation conducted before the introduction of forced-air warming clearly showed a reduction in the rates of infection. Additionally, the widespread acceptance that forced-air warming reduces the rate of infection has only been demonstrated in colorectal surgery.[36]

Until the disruptive effects of forced-air warming on ventilation can be fully evaluated with regard to affecting the sterility of the surgical site, the use of air-free patient warming alternatives might be recommended for procedures involving implants carried out in ultra-clean theatres.

Supplementary material

A video demonstrating forced-air warming is available with the electronic version of this article on our website at www.jbjs.org.uk

The author or one or more of the authors have received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article.

References

1. **Lidwell OM.** Clean air at operation and subsequent sepsis in the joint. *Clin Orthop* 1986;211:91–102.
2. **Petty W, Spanier S, Shuster JJ, Silverthorne C.** The influence of skeletal implants on incidence of infection: experiments in a canine model. *J Bone Joint Surg [Am]* 1985;67-A:1236–1244.
3. **Lidwell OM, Elson RA, Lowbury EJ, et al.** Ultraclean air and antibiotics for prevention of postoperative infection: a multicenter study of 8,052 joint replacement operations. *Acta Orthop Scand* 1987;58:4–13.
4. **Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR.** Guideline for prevention of surgical site infection, 1999: Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. *Am J Infect Control* 1999;27:97–132.
5. **No authors listed.** Arizant. Bair Hugger® Therapy: Warming Units & Accessories. http://www.arizant.com/us/bairhuggertherapy/warmingunits (date last accessed 13 July 2011).
6. **Bayazit Y, Sparrow EM.** Energy efficiency comparison of forced-air versus resistance heating devices for perioperative hypothermia management. *Energy* 2010;35:1211–1215.
7. **Chow TT, Yang XY.** Ventilation performance in the operating theatre against airborne infection: numerical study on an ultra-clean system. *J Hosp Infect* 2005;59:138–147.
8. **Wong PF, Kumar S, Leaper DJ.** Systemic warming as an adjunct to resuscitation in peritonitis: a pilot, randomized controlled trial. *Surg Infect (Larchmt)* 2007;8:387–395.
9. **Wong PF, Kumar S, Bohra A, Whetter D, Leaper DJ.** Randomized clinical trial of perioperative systemic warming in major elective abdominal surgery. *Br J Surg* 2007;94:421–426.
10. **Ng V, Lai A, Ho V.** Comparison of forced-air warming and electric heating pad for maintenance of body temperature during total knee replacement. *Anaesthesia* 2006;61:1100–1104.
11. **Janke E, Pilkington SN, Smith DC.** Evaluation of two warming systems after cardiopulmonary bypass. *Br J Anaesth* 1996;77:268–270.
12. **Kimberger O, Held C, Stadelmann K, et al.** Resistive polymer versus forced-air warming: comparable heat transfer and core rewarming rates in volunteers. *Anesth Analg* 2008;107:1621–1626.
13. **Negishi C, Hasegawa K, Mukai S, et al.** Resistive-heating and forced-air warming are comparably effective. *Anesth Analg* 2003;96:1683–1687.
14. **Matsuzaki Y, Matsukawa T, Ohki K, et al.** Warming by resistive heating maintains perioperative normothermia as well as forced air heating. *Br J Anaesth* 2003;90:689–691.
15. **No authors listed.** Hospital Technical Memorandum (HTM) 2025. Ventilation of healthcare premises, 1994. http://www.spaceforhealth.nhs.uk/ (date last accessed 14 September 2011).
16. **Whyte W, Shaw BH.** The effect of obstructions and thermals in laminar-flow systems. *J Hyg (Lond)* 1974;72:415–423.
17. **Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG.** CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. *Infect Control Hosp Epidemiol* 1992;13:606–608.
18. **Olsen MA, Nepple JJ, Riew KD, et al.** Risk factors for surgical site infection following orthopaedic spinal operations. *J Bone Joint Surg [Am]* 2008;90-A:62–69.
19. **Friberg B.** Ultraclean laminar airflow ORs. *AORN J* 1998;67:841–851.
20. **Brohus H, Balling KD, Jeppesen D.** Influence of movements on contaminant transport in an operating room. *Indoor Air* 2006;16:356–372.
21. **Chow TT, Yang XY.** Ventilation performance in operating theatres against airborne infection: review of research activities and practical guidance. *J Hosp Infect* 2004;56:85–92.
22. **Whyte W, Vesley D, Hodgson R.** Bacterial dispersion in relation to operating room clothing. *J Hyg (Lond)* 1976;76:367–378.
23. **Lidwell OM.** Air, antibiotics and sepsis in replacement joints. *J Hosp Infect* 1988;11(Suppl):18–40.
24. **Hooper G, Rothwell AG, Frampton C, Wyatt MC.** Does the use of laminar flow and space suits reduce early deep infection after total hip and knee replacement?: the ten-year results of the New Zealand Joint Registry. *J Bone Joint Surg [Br]* 2011;93-B:85–90.
25. **Jensen CD, Steval A, Partington PF, Reed MR, Muller SD.** Return to theatre following total hip and knee replacement, before and after the introduction of rivaroxaban: a retrospective cohort study. *J Bone Joint Surg [Br]* 2011;93-B:91–95.
26. **Zink RS, Iaizzo PA.** Convective warming therapy does not increase the risk of wound contamination in the operating room. *Anesth Analg* 1993;76:50–53.
27. **Huang JKC, Shah EF, Vinodkumar N, Hegarty MA, Greatorex RA.** The Bair Hugger patient warming system in prolonged vascular surgery: an infection risk? *Crit Care* 2003;7:13–16.
28. **Albrecht M, Gauthier RL, Belani K, Litchy M, Leaper D.** Forced-air warming blowers: an evaluation of filtration adequacy and airborne contamination emissions in the operating room. *Am J Infect Control* 2011;39:321–328.
29. **Leaper D, Albrecht M, Gauthier R.** Forced-air warming: a source of airborne contamination in the operating room? *Orthop Rev* 2009;1:e28.
30. **Avidan MS, Jones N, Ing R, et al.** Convection warmers: not just hot air. *Anaesthesia* 1997;52:1073–1076.
31. **Baker N, King D, Smith EG.** Infection control hazards of intraoperative forced air warming. *J Hosp Infect* 2002;51:153–154.
32. **Bernards AT, Harinck HIJ, Dijkshoorn L, van der Reijden TJK, van den Broek PJ.** Persistent Acinetobacter baumannii?: look inside your medical equipment. *Infect Control Hosp Epidemiol* 2004;25:1002–1004.
33. **Tumia N, Ashcroft GP.** Convection warmers: a possible source of contamination in laminar airflow operating theatres? *J Hosp Infect* 2002;52:171–174.
34. **Miner AL, Losina E, Katz JN, Fossel AH, Platt R.** Deep infection after total knee replacement: impact of laminar airflow systems and body exhaust suits in the modern operating room. *Infect Control Hosp Epidemiol* 2007;28:222–226.
35. **Brandt C, Hott, Sohr D, et al.** Operating room ventilation with laminar airflow shows no protective effect on the surgical site infection rate in orthopedic and abdominal surgery. *Ann Surg* 2008;248:695–700.
36. **Kurz A, Sessler DI, Lenhardt R.** Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization: study of wound infection and temperature group. *N Engl J Med* 1996;334:1209–1215.

EXHIBIT DX2

TO DECLARATION OF BENJAMIN W. HULSE IN SUPPORT OF DEFENDANTS' MOTION FOR RECONSIDERATION OF THE COURT'S DECEMBER 13, 2017 ORDER ON GENERAL CAUSATION

PART I

GENERAL ASSEMBLY

Continued...

for the active operating room, such as those prevalent in pharmacy and clean room settings, should be considered in the future.

REFERENCES

[1] Shohat N, Parvizi J. Prevention of periprosthetic joint infection: examining the recent guidelines. J Arthroplasty. 2017;32:2040–2046. doi:10.1016/j.arth.2017.02.072.

[2] Parvizi J, Shohat N, Gehrke T. Prevention of periprosthetic joint infection: new guidelines. Bone Joint J. 2017;99-B:3–10. doi:10.1302/0301-620X.99B4.BJJ-2016-1212.R1.

[3] Küçükdurmaz F, Parvizi J. The prevention of periprosthetic joint infections. Open Orthop J. 2016;10:589–599. doi:10.2174/1874325001610010589.

[4] Charnley J, Eftekhar N. Postoperative infection in total prosthetic replacement arthroplasty of the hip-joint. With special reference to the bacterial content of the air of the operating room. Br J Surg. 1969;56:641–649.

[5] Turner RS. Laminar air flow. Its original surgical application and long-term results. J Bone Joint Surg Am. 1974;56:430–435.

[6] Dharan S, Pittet D. Environmental controls in operating theatres. J Hosp Infect. 2002;51:79–84.

[7] Iudicello S, Fadda A. A road map to a comprehensive regulation on ventilation technology for operating rooms. Infect Control Hosp Epidemiol. 2013;34:858–860. doi:10.1086/671261.

[8] James M, Khan WS, Nannaparaju MR, Bhamra JS, Morgan-Jones R. Current evidence for the use of laminar flow in reducing infection rates in total joint arthroplasty. Open Orthop J. 2015;9:495–498. doi:10.2174/1874325001509010495.

[9] Fitzgerald RH. Total hip arthroplasty sepsis. Prevention and diagnosis. Orthop Clin North Am. 1992;23:259–264.

[10] Lidwell OM, Lowbury EJ, Whyte W, Blowers R, Stanley SJ, Lowe D. Effect of ultraclean air in operating rooms on deep sepsis in the joint after total hip or knee replacement: a randomised study. Br Med J (Clin Res Ed). 1982;285:10–14.

[11] Kakwani RG, Yohannan D, Wahab KH. The effect of laminar air-flow on the results of Austin-Moore hemiarthroplasty. Injury. 2007;38:820–823. doi:10.1016/j.injury.2006.09.025.

[12] Marotte JH, Lord GA, Blanchard JP, Guillamon JL, Samuel P, Servant JP, et al. Infection rate in total hip arthroplasty as a function of air cleanliness and antibiotic prophylaxis. 10-year experience with 2,384 cementless Lord madreporic prostheses. J Arthroplasty. 1987;2:77–82.

[13] van Griethuysen AJ, Spies-van Rooijen NH, Hoogenboom-Verdegaal AM. Surveillance of wound infections and a new theatre: unexpected lack of improvement. J Hosp Infect. 1996;34:99–106.

[14] Breier A-C, Brandt C, Sohr D, Geffers C, Gastmeier P. Laminar airflow ceiling size: no impact on infection rates following hip and knee prosthesis. Infect Control Hosp Epidemiol. 2011;32:1097–1102. doi:10.1086/662182.

[15] Singh S, Reddy S, Shrivastava R. Does laminar airflow make a difference to the infection rates for lower limb arthroplasty: a study using the National Joint Registry and local surgical site infection data for two hospitals with and without laminar airflow. Eur J Orthop Surg Traumatol. 2017;27:261–265. doi:10.1007/s00590-016-1852-1.

[16] Pinder EM, Bottle A, Aylin P, Loeffler MD. Does laminar flow ventilation reduce the rate of infection? an observational study of trauma in England. Bone Joint J. 2016;98-B:1262–1269. doi:10.1302/0301-620X.98B9.37184.

[17] Brandt C, Hott U, Sohr D, Daschner F, Gastmeier P, Rüden H. Operating room ventilation with laminar airflow shows no protective effect on the surgical site infection rate in orthopedic and abdominal surgery. Ann Surg. 2008;248:695–700. doi:10.1097/SLA.0b013e31818b757d.

[18] Hooper GJ, Rothwell AG, Frampton C, Wyatt MC. Does the use of laminar flow and space suits reduce early deep infection after total hip and knee replacement?: the ten-year results of the New Zealand Joint Registry. J Bone Joint Surg Br. 2011;93:85–90. doi:10.1302/0301-620X.93B1.24862.

[19] Tayton ER, Frampton C, Hooper GJ, Young SW. The impact of patient and surgical factors on the rate of infection after primary total knee arthroplasty: an analysis of 64,566 joints from the New Zealand Joint Registry. Bone Joint J. 2016;98-B:334–340. doi:10.1302/0301-620X.98B3.36775.

[20] Heating and ventilation of health sector buildings (HTM 03-01). GOVUK n.d. https://www.gov.uk/government/publications/guidance-on-specialised-ventilation-for-healthcare-premises-parts-a-and-b (accessed July 12, 2018).

[21] Whyte W, Hodgson R, Tinkler J. The importance of airborne bacterial contamination of wounds. J Hosp Infect. 1982;3:123–135.

[22] Gastmeier P, Breier AC, Brandt C. Influence of laminar airflow on prosthetic joint infections: a systematic review. J Hosp Infect. 2012;81:73–78. doi:10.1016/j.jhin.2012.04.008.

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QUESTION 2: Does the use of forced air warming (FAW) during orthopaedic procedures increase the risk of subsequent surgical site infections/periprosthetic joint infections (SSIs/PJIs)?

RECOMMENDATION: There is no evidence to definitively link FAW to an increased risk of SSIs/PJIs. Alternative methods of warming can be effective and may be used.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 93%, Disagree: 2%, Abstain: 5% (Super Majority, Strong Consensus)

RATIONALE

Maintaining intraoperative normothermia has been shown to reduce perioperative complications including SSI. FAW represents one of the most widely-used methods to prevent hypothermia and maintain intraoperative normothermia. Intraoperative hypothermia has been linked to increased mortalities and morbidities, longer hospital stays, increased requirements for blood transfusion and increased SSI rates. The SSI prevention effects have not been demonstrated in implant surgery, such as total knee arthroplasty (TKA), total hip arthroplasty (THA) and total shoulder arthroplasty (TSA). There has been a concern in the literature about possible contamination of the operating room (OR) air and surgical field with these devices, and subsequent potential increased risk of SSI, especially PJI. Conductive fabric blankets (CFBs) have been suggested as an alternative for intraoperative warming.

Several experimental studies raised a concern for the possibility of intraoperative contamination caused by FAW. McGovern et al. compared FAW and conductive fabric warming (CFW) devices in a simulation of hip and spine surgery with a mannequin used as a patient [1]. They used bubbles generated at the floor and at the mannequin's head to monitor flow of air in the simulated theater and detected significantly increased bubbles close to the surgical field with the use of the FAW devices. They also conducted a clinical review of their infection data between a twenty-month period when FAW devices were used vs. a seven-month period where CFW devices were used, and found a statistically higher rate of deep SSI with the use of the FAW device. The authors noted, however, that their observational study did not account for infection control procedures that changed over the study period or account for several possible differences in patient risk factors, such as obesity and fitness for surgery. Other studies of the same cohorts by these researchers revealed potential impacts unrelated to the change in warming modality, including thromboprophylaxis [2] and methicillin-sensitive *Staphylococcus aureus* screening [3]. Legg et al. measured changes in temperature and air particles at the surgical site in a simulated OR setup with a volunteer patient simulator [4]. They found statistically significant increases in temperature and particle counts with the

use of FAW compared to controls or radiant warming devices. In a follow-up study on a simulated TKA set-up, the authors used a bubble generator with a digital camera to actually visualize airflow disruptions caused by FAW [5].

Similar to the prior study, they showed a significant increase in particle counts at the surgical site and in drape temperatures. They also identified a substantial disruption in the unidirectional airflow when FAW was used. Dasari et al. conducted an experiment where a mannequin was used as a patient and temperature was measured at multiple different heights and locations with the use of FAW, a conductive blanket or a resistive mattress [6]. They found significantly greater temperature increases caused by FAW at patient height locations, whereas, temperatures measured at other heights (floor, head and ceiling) were similar among the three warming devices. They concluded that FAW generates convection current activity in the vicinity of the surgical site which may disrupt laminar air flow. Belani et al. conducted a study with a mannequin draped for a TKA in an orthopaedic room and a bubble generator placed at the head to visualize air currents [7]. Bubbles were counted on sequential photographs at the surgical field and compared between FAW and CFW. The authors found significantly increased bubble counts over the surgical site with FAW and time-lapse photography identified convection currents mobilizing air from the mannequin's head over the drapes and into the surgical field. A recent predictive fluid flow simulation conducted by He et al. on a computer aided design OR showed significant disruption in airflow caused by FAW with a displacement of squames from the floor into the surgical field [8].

Tumia et al. quantified bacterial counts in air samples taken in empty ORs, during normal surgical operations prior to turning the FAW device on, and 15 minutes after turning the warmer on [9]. They had low study numbers to reach statistical significance, but they observed an increase in bacterial counts during regular surgical operations with the warmer off compared to the empty OR and a further increase after turning the warmer on. They concluded that most of the contamination of OR air is secondary to the presence of surgical staff and OR traffic, and that FAW increases contamination to a lesser extent, but this is likely not of clinical significance given that the counts seen were still well below recommendations for ultra-clean air theaters. Albrecht et al. evaluated filter efficiency in the air blower of FAW devices and found that the intake filters used in air blowers were far from optimal efficiency which resulted in colonization of the internal parts of the device [10,11]. They cultured organisms such as *Staphylococcus aureus* and coagulase-negative *Staphylococcus*, which are known to be the major pathogens in total joint arthroplasty. Avidan et al. sampled air coming out of blowers and also found positive cultures in 4 out of 10 devices [12]. However, after connecting the perforated blanket to the air blower and sampling the air coming out underneath the blankets, no organisms grew.

On the other hand, several studies have failed to demonstrate any increased contamination with the use of FAW. Sharp et al. performed a surgical simulation using patients with psoriasis, who are known to have increased shedding of skin [13]. They utilized slit-air sampling and simulated regular OR activity. No bacterial colonies were grown, leading the authors to conclude that FAW did not result in the contamination of the surgical site. Sessler et al. evaluated the effect of FAW on operative room air in laminar airflow conditions using volunteer subjects in an OR with simulated surgical set-up and heated mannequins to simulate OR personnel [14]. A smoke plume was used to visualize airflow and revealed that FAW did not induce any upward draft or any disruption in the normal downward movement of sterile air. A particle counter was used to evaluate changes in particle concentrations near a theoretical incision site. No significant differences were found between having the FAW device off, on ambient air or on warm air. All scenarios had particle counts below stringent criteria established in Europe for the evaluation of adequate function of laminar flow in operating rooms.

Moretti et al. evaluated the effect of FAW on air quality during THA procedures with the use of an air-sampling device with agar plates [15]. No differences in bacterial loads were noted at several positions of the surgical field with or without the use of FAW. Memarzadeh et al. reported computational fluid dynamics and particle tracking studies conducted by the National Institutes of Health to assess whether FAW devices lead to contamination of the surgical site [16]. They found no increased squame deposition from potential contaminant sources due to the FAW device in laminar flow theater situations in their models. Zink et al. evaluated air quality in rooms with volunteers lying down covered by surgical drapes with culture plates placed on their abdomen while FAW was turned on for two hours [17]. Results were compared to a two-hour period where the warmer was turned off. No statistically significant difference was identified between the two situations. Shirozu et al. looked at the effect of FAW on airflow in a simulated operative setting with the use of an ultrasonic anemometer, smoke and laser light [18]. The authors found that downward laminar flow efficiently counteracted the upward airflow caused by FAW blankets and concluded that contamination of the surgical field is not likely in the presence of adequate laminar flow. In a study from the veterinarian literature, two groups of surgical patients were compared (one with use of FAW blankets and one without) [19]. Surgical drapes were swabbed and aerobic cultures were obtained. No difference in positive cultures was noted.

Oguz et al. recently conducted a prospective study where orthopaedic patients were randomized to receive either a FAW blanket or a CFW [20]. They performed a multivariate analysis looking at the effect of multiple factors on the number of bacteria in the OR air and on the field as measured by agar plates positioned at different locations in the room, and nitrocellulose plates placed on the instrument table. These factors included the type of warming device in addition to the presence of laminar airflow, the number of operating room personnel and the operative time. While increased surgical time and absence of laminar flow significantly affected bacterial counts, the type of warming device used did not.

Sikka and Prielipp published a focused review of the literature in the Journal of Bone and Joint Surgery and concluded that there is not enough evidence to support or disprove a link between FAW and PJI [21]. They did list recommendations that need to be followed for proper use of the devices including frequent filter changes, calibration and always using the device with the accompanying blanket. Kellam et al. in a comprehensive review for the Association of Perioperative Registered Nurses (AORN) failed to identify conclusive evidence for an increased risk of SSI with the use of FAW and recommended continued use of these devices [22]. Wood et al. conducted a similar review and concluded that FAW does contaminate ultra-clean air in the operating room, but found no definite link to an increased rate of SSIs [23]. They recommended considering alternative warming systems when contamination of the surgical field is deemed to be critical. In a more recent systematic review that encompassed a total of 1,965 patients and 8 studies, Haeberle et al. concluded that there was an absence of evidence to support an increased rate of SSI with the use of FAW blankets [24].

Sandoval et al. compared FAW vs. CFW in its ability to prevent hypothermia in 120 THA and TKA surgeries [25]. There were 60 patients in each group and they concluded that FAW and CFB were equally as effective at maintaining core temperatures during and after surgery. There were no reported SSIs in either group. This study was a quality improvement project and not powered to show a clinically significant difference in infection rates.

In conclusion, the literature is conflicting and there is still a lack of strong evidence linking FAW to increased risk of SSI. In light of this, while we recognize the theoretical risk posed by FAW, we cannot recommend discontinuing the use of these devices at this time. We do, however, recommend following the manufacturer's instructions and frequently changing the filters, making sure the devices are calibrated and most importantly using the devices only with the appropriate perforated blanket. Other alternative warming methods can be used. We recommend a randomized prospective trial to answer the index question, and a pilot is underway. (ISRCTN 74612906)

REFERENCES

[1] McGovern PD, Albrecht M, Belani KG, et al. Forced-air warming and ultra-clean ventilation do not mix: an investigation of theatre ventilation, patient warming and joint replacement infection in orthopaedics. J Bone Joint Surg Br. 2011;93:1537–1544. doi:10.1302/0301-620X.93B11.27124.

[2] Jensen C.D., Steval A, Partington, et al. Return to theatre following total hip and knee replacement, before and after the introduction of rivoraxaban. A retrospective cohort study. J Bone Joint Surg Br. 2011;93:91–95. doi: 10.1302/0301-620X.93B1.24987.

[3] Jeans E, Holleyman R, Tate D et al. Methicillin sensitive staphylococcus aureus screening and decolonisation in elective hip and knee arthroplasty. J Infect. 2018; Jun 19 pii:S0163-4453(18)30180-4. doi:10.1016/j.jnf.2018.05.012 .

[4] Legg AJ, Cannon T, Hamer AJ. Do forced air patient-warming devices disrupt unidirectional downward airflow? J Bone Joint Surg Br. 2012;94:254–256. doi:10.1302/0301-620X.94B2.27562.

[5] Legg AJ, Hamer AJ. Forced-air patient warming blankets disrupt unidirectional airflow. Bone Joint J. 2013;95-B:407–410. doi:10.1302/0301-620X.95B3.29121.

[6] Dasari KB, Albrecht M, Harper M. Effect of forced-air warming on the performance of operating theatre laminar flow ventilation. Anaesthesia. 2012;67:244–249. doi:10.1111/j.1365-2044.2011.06983.x.

[7] Belani KG, Albrecht M, McGovern PD, Reed M, Nachtsheim C. Patient warming excess heat: the effects on orthopedic operating room ventilation performance. Anesth Analg. 2013;117:406–411. doi:10.1213/ANE.0b013e31825f81e2.

[8] He X, Karra S, Paksereshт P, Apte SV, Elghobashi S. Effect of heated-air blanket on the dispersion of squames in an operating room. Int J Numer Methods Biomed Eng. January 2018. doi:10.1002/cnm.2960.

[9] Tumia N, Ashcroft GP. Convection warmers—a possible source of contamination in laminar airflow operating theatres? J Hosp Infect. 2002;52:171–174.

[10] Albrecht M, Gauthier RL, Belani K, Litchy M, Leaper D. Forced-air warming blowers: An evaluation of filtration adequacy and airborne contamination emissions in the operating room. Am J Infect Control. 2011;39:321–328. doi:10.1016/j.ajic.2010.06.011.

[11] Albrecht M, Gauthier R, Leaper D. Forced-air warming: a source of airborne contamination in the operating room? Orthop Rev. 2009;1(2). doi:10.4081/or.2009.e28.

[12] Avidan MS, Jones N, Ing R, Khoosal M, Lundgren C, Morrell DF. Convection warmers—not just hot air. Anaesthesia. 1997;52:1073–1076.

[13] Sharp RJ, Chesworth T, Fern ED. Do warming blankets increase bacterial counts in the operating field in a laminar-flow theatre? J Bone Joint Surg Br. 2002;84:486–488.

[14] Sessler DI, Olmsted RN, Kuelpmann R. Forced-air warming does not worsen air quality in laminar flow operating rooms. Anesth Analg. 2011;113:1416–1421. doi:10.1213/ANE.0b013e318230b3cc.

[15] Moretti B, Larocca AMV, Napoli C, et al. Active warming systems to maintain perioperative normothermia in hip replacement surgery: a therapeutic aid or a vector of infection? J Hosp Infect. 2009;73:58–63. doi:10.1016/j.jhin.2009.06.006.

[16] Memarzadeh F. Active warming systems to maintain perioperative normothermia in hip replacement surgery. J Hosp Infect. 2010;75:332–333. doi:10.1016/j.jhin.2010.02.006.

[17] Zink RS, Iaizzo PA. Convective warming therapy does not increase the risk of wound contamination in the operating room. Anesth Analg. 1993;76:50–53.

[18] Shirozu K, Kai T, Setoguchi H, Ayagaki N, Hoka S. Effects of forced air warming on airflow around the operating table. Anesthesiology. 2018;128:79–84. doi:10.1097/ALN.0000000000001929.

[19] Occhipinti LL, Hauptman JG, Greco JJ, Mehler SJ. Evaluation of bacterial contamination on surgical drapes following use of the Bair Hugger(®) forced air warming system. Can Vet J Rev Veterinaire Can. 2013;54:1157–1159.

[20] Oguz R, Diab-Elschahawi M, Berger J, et al. Airborne bacterial contamination during orthopedic surgery: A randomized controlled pilot trial. J Clin Anesth. 2017;38:160–164. doi:10.1016/j.jclinane.2017.02.008.

[21] Sikka RS, Prielipp RC. Forced air warming devices in orthopaedics: a focused review of the literature. J Bone Joint Surg Am. 2014;96(24):e200. doi:10.2106/JBJS.N.00054.

[22] Kellam MD, Dieckmann LS, Austin PN. Forced-air warming devices and the risk of surgical site infections. AORN J. 2013;98:354–366; quiz 367–369. doi:10.1016/j.aorn.2013.08.001.

[23] Wood AM, Moss C, Keenan A, Reed MR, Leaper DJ. Infection control hazards associated with the use of forced-air warming in operating theatres. J Hosp Infect. 2014;88:132–140. doi:10.1016/j.jhin.2014.07.010.

[24] Haeberle HS, Navarro SM, Samuel LT, et al. No evidence of increased infection risk with forced-air warming devices: a systematic review. Surg Technol Int. 2017;31:295–301.

[25] Sandoval MF, Mongan PD, Dayton MR, Hogan CA. Safety and efficacy of resistive polymer versus forced air warming in total joint surgery. Patient Saf Surg. 2017;11:11.

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QUESTION 3: Does the operating room (OR) temperature affect the rate of subsequent surgical site infections/periprosthetic joint infections (SSIs/PJIs)?

RECOMMENDATION: The OR temperature may affect core body temperature, which could potentially affect the rates of subsequent SSIs/PJIs. Thus, all efforts should be made to maintain an optimal OR temperature.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 88%, Disagree: 8%, Abstain: 4% (Super Majority, Strong Consensus)

RATIONALE

Multiple OR varaibles are known to influence the rates of SSIs/PJIs in patients undergoing orthopaedic procedures. Some of the important issues in the OR are the status of the ventilation system, environmental contamination, including air as well as surface contamination in association with humidity, and temperatures that are known factors sustaining microorganism growth. Clinically used ventilation systems are able to reduce the number of colony forming units (CFUs) near the surgical field. However, systems using vertical laminar airflow and those relying on a newly developed temperature-controlled air flow have been shown to achieve better suppression of environmental contamination that is even more efficacious than classical laminar air flow systems.

Recently-published studies have demonstrated correlations between seasonal temperature changes and SSI rates. SSIs peaked during the warmer season and were lowest in the winter and this in itself could include a multitude of additional environmental factors.

The currently-available literature has not established the ideal OR temperature range, but suggests that temperatures around or below 24°C are preferable. In some countries (e.g., Germany), International Organization for Standardization (ISO) norms describe a

need to select OR temperatures between 18°C and 24°C. We are not aware of any studies about a lower temperature boundary showing adverse effects concerning wound healing, cardiovascular circulation, etc.

Another factor associated with increased temperatures in the OR setting are the increase in transpiration rates among the OR personnel, specifically the surgeon, who may contaminate the surgical field with sweat.

Everett et al. reported that the incidence of SSIs increased when the ventilation system progressively deteriorated. They found with new improved ventilation systems the infections returned to baseline rates. The control of temperature and humidity is important mainly for the comfort of the OR personnel (low-quality study) [1].

Alfonso-Sanchez et al. conducted a longitudinal prospective study to identify the influence of OR environmental factors on subsequent SSIs. Risk factors related to the OR included the level of fungi and bacterial contamination, temperature and humidity, as well as air renewal and differential air pressure. Patient-related variables assessed included age, sex, comorbidities, nutrition level and transfusion. Other factors were antibiotic prophylaxis, electric versus manual shaving, American Society of Anaesthesiologists physical status classification, type of intervention, duration of the intervention and preoperative stay [2]. Superficial SSIs were most often associated with environmental factors, such as environmental contamination by fungi (from two colony-forming units), by bacteria, as well as surface contamination. The environmental factors studied, including the OR temperatures, were found to influence the rates of subsequent SSIs. For example, when there was no contamination in the OR, no SSIs were detected. Significant risk factors in superficial SSIs were environmental contamination by fungi (≥ 6 CFU/m³, with a relative risk (RR) of 6.2), bacteria, as well as surface contamination by both fungi and bacteria. Also important were humidity, differential pressure and OR temperatures. The OR temperature was associated with superficial SSIs, but not deep SSIs [2].

Fu Shaw et al. noted that the bacterial colony count increased by 9.4 CFU/m³ with each additional 1°C rise at room temperature ($p = 0.018$) [3]. Another study by Alsved et al. compared two commonly-used ventilation systems (vertical laminar airflow (LAF) and turbulent mixed airflow (TMA)) with a newly-developed ventilation technique and temperature-controlled airflow (TAF), measuring CFU concentrations at three OR locations. They also evaluated comfort on the operating team. The study found that only LAF and TAF resulted in less than 10 CFU/mL at all measurement locations in the room during surgery. Median values of cfu/m³ close to the wound (250 samples) were 0 for LAF, 1 for TAF and 10 for TMA. Peripherally in the room, the CFU concentrations were lowest for TAF. The CFU concentrations did not scale proportionally with airflow rates. Compared with LAF, the power consumption of TAF was 28% lower and there was significantly less disturbance from noise and draught. [4].

Anthony et al. analyzed 760,283 procedures (total knee arthroplasty (TKA) 424,104, total hip arthroplasty (THA) 336,179) for the influence of seasonal temperatures on SSIs. Their models indicate that SSI risks were highest for patients discharged in June, and lowest for those discharged December. For TKA, the odds of 30-day readmission for SSIs were 30.5% higher at the peak compared to the nadir time (95% confidence interval (CI) 20 to 42). For THA, the seasonal increase in SSIs was 19% (95% CI 9 to 30). (High-quality study) [5].

Another study by Anthony et al. described a highly seasonal variability of SSI, with the highest SSI incidence in August and the lowest in January. During the study period, there were 26.5% more cases in August than in January (95% CI, 23.3 to 29.7). Controlling for demographic and hospital-level characteristics, the odds of a primary SSI readmission increased by roughly 2.1% per 2.8°C (5°F) increase in the average monthly temperature. Specifically, the highest temperature group (> 32.2°C [> 90°F]) was associated with an increase in the odds for an SSI readmission by 28.9% (95% CI, 20.2 to 38.3) compared to lower temperatures (< 4.4°C [< 40°F]) (moderate-quality study) [6].

Mills et al. concluded that the sweating surgeon may most likely contaminate the surgical field as a result of elevated OR temperatures [7].

Based on the available evidence, it appears that OR tempreature is an important enviromental factor that needs to be optimally controlled during surgical procedures. There is an indirect link between the OR temperatures and the potential for subsequent SSIs/PJIs.

REFERENCES

[1] Everett WD, Kipp H. Epidemiologic observations of operating room infections resulting from variations in ventilation and temperature. Am J Infect Control. 1991;19:277–282.

[2] Alfonso-Sanchez JL, Martinez IM, Martín-Moreno JM, González RS, Botia F. Analyzing the risk factors influencing surgical site infections: the site of environmental factors. Can J Surg. 2017;60:155–161.

[3] Fu Shaw L, Chen IH, Chen CS, Wu HH, Lai LS, Chen YY, et al. Factors influencing microbial colonies in the air of operating rooms. BMC Infect Dis. 2018;18:4. doi:10.1186/s12879-017-2928-1.

[4] Alsved M, Civilis A, Ekolind P, Tammelin A, Andersson AE, Jakobsson J, et al. Temperature-controlled airflow ventilation in operating rooms compared with laminar airflow and turbulent mixed airflow. J Hosp Infect. 2018;98:181–190. doi:10.1016/j.jhin.2017.10.013.

[5] Anthony CA, Peterson RA, Sewell DK, Polgreen LA, Simmering JE, Callaghan JJ, et al. The seasonal variability of surgical site infections in knee and hip arthroplasty. J Arthroplasty. 2018;33:510–514.e1. doi:10.1016/j.arth.2017.10.043.

[6] Anthony CA, Peterson RA, Polgreen LA, Sewell DK, Polgreen PM. The seasonal variability in surgical site infections and the association with warmer weather: a population-based investigation. Infect Control Hosp Epidemiol. 2017;38:809–816. doi:10.1017/ice.2017.84.

[7] Mills SJ, Holland DJ, Hardy AE. Operative field contamination by the sweating surgeon. Aust N Z J Surg. 2000;70:837–839.

Authors: Georgios Komnos, Koji Yamada

QUESTION 4: Does perioperative normothermia affect the rate of subsequent surgical site infections/periprosthetic joint infections (SSIs/PJIs)?

RECOMMENDATION: Based on data from general surgery and other surgical disciplines, normothermia has been found to be an important factor during the perioperative period, in order to minimize the risks of subsequent infections. Although evidence in orthopaedic surgery is sparse, we recommend that normothermia also be maintained in patients undergoing orthopaedic procedures.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 97%, Disagree: 1%, Abstain: 2% (Unanimous, Strongest Consensus)

RATIONALE

Medications used during general anesthesia, such as inhaled and intravenous agents as well as opioids, alter the ability for the body to thermoregulate which may result in hypothermia [1]. Hypothermia can also result from the use of neuraxial anesthesia, except with peripheral nerve blocks [1]. Several animal studies have demonstrated that intraoperative hypothermia may decrease resistance to some pathogens, such as *Escherichia coli* (*E. coli*) and *Staphylococcus aureus* [2,3]. Hypothermia and secondary vasoconstriction may also lead to reduced oxygen delivery to tissues, increasing the risks of infectious complications [4–6]. Several well-designed studies have attributed a substantial decrease in SSI rates in colorectal and non-orthopaedic clean surgeries with normothermia [5,6]. Therefore, current guidelines from the World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) recommend maintaining perioperative normothermia to reduce the risk of SSIs and other complications associated with surgery [7,8]. However, there is a paucity of published literature regarding normothermia in orthopaedic procedures.

In a recent observational study evaluating the role of hypothermia in hip fractures, the incidence of perioperative hypothermia was 17%. After multivariate logistic regression analysis, hypothermia was associated with increased risk of periprosthetic joint infection (PJI) (odds ratio (OR): 3.30, 95% confidence interval (CI) 1.19 to 9.14, $p = .022$) [9]. In contrast, from another observational study evaluating total hip and knee arthroplasties, no statistically significant associations were found between hypothermia and PJIs or SSIs in univariate analysis [10]. Observational studies [10–13] have associated hypothermia with increased blood loss and transfusion rates, which may subsequently lead to increased risks for PJIs or SSIs. However, there are no randomized controlled trials (RCTs) that support nor discourage normothermia in total joint arthroplasty (TJA) or other orthopaedic procedures in relation to SSIs or PJIs.

There are several RCTs that have been performed outside of orthopaedics, which support the use of warming devices in the operating room and during the surgical procedure for the purposes of reducing SSIs [5,6]. Kurz et al. evaluated the importance of maintaining perioperative normothermia with additional warming in major colorectal surgery patients [5]. The mean final intraoperative core temperature was higher in those with additional warming compared with those without (36.6 vs. 34.7 °C, $p < 0.001$). Patients assigned to additional warming demonstrated a significant decrease in SSI rates by receiving forced-air warming blankets combined with fluid warming (6 vs. 19%, $p = 0.009$). In another RCT, Melling et al. evaluated patients undergoing non-orthopaedic clean surgeries and identified a substantial role of pre-warming in preventing SSI [6]. They showed that warming the patient for at least 30 minutes before surgery led to a reduction in infection rate from 14 to 5% ($p = 0.001$) [6].

The safest and most effective mode of maintaining intraoperative normothermia remains unknown. Some recent studies have raised potential issues with the use of forced-air warming systems that may disrupt the laminar airflow (LAF) in operating rooms and increase risks for SSIs [14–16]. But, from a recent experimental study, disruption of airflow produced by forced-air warming was well-counteracted by downward LAF from the ceiling [17]. There are no studies which provide high-level evidence that warming systems may increase infection rates.

In summary, achieving normothermia by using warming devices in the operating room and during the surgical procedure seems to play an important role in decreasing the risks of subsequent infections. However, this evidence mainly derives from non-orthopaedic literature. Further research is needed to establish correlation between patient's temperature and SSIs in the field of orthopaedic surgery, including TJAs.

REFERENCES

[1] Sessler DI. Perioperative thermoregulation and heat balance. Lancet. 2016;387:2655–2664. doi:10.1016/S0140-6736(15)00981-2.

[2] Sheffield CW, Sessler DI, Hunt TK. Mild hypothermia during isoflurane anesthesia decreases resistance to E. coli dermal infection in guinea pigs. Acta Anaesthesiol Scand. 1994;38:201–205.

[3] Sheffield CW, Sessler DI, Hunt TK, Scheuenstuhl H. Mild hypothermia during halothane-induced anesthesia decreases resistance to Staphylococcus aureus dermal infection in guinea pigs. Wound Repair Regen. 1994;2:48–56. doi:10.1046/j.1524-475X.1994.20108.x.

[4] Warttig S, Alderson P, Campbell G, Smith AF. Interventions for treating inadvertent postoperative hypothermia. Cochrane Database Syst Rev. 2014:CD009892. doi:10.1002/14651858.CD009892.pub2.

[5] Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. N Engl J Med. 1996;334:1209–1215. doi:10.1056/NEJM199605093341901.

[6] Melling AC, Ali B, Scott EM, Leaper DJ. Effects of preoperative warming on the incidence of wound infection after clean surgery: a randomised controlled trial. Lancet. 2001;358:876–880. doi:10.1016/S0140-6736(01)06071-8.

[7] Berrios-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, et al. Centers for Disease Control and Prevention guideline for the prevention of surgical site infection, 2017. JAMA Surg. 2017;152:784–791. doi:10.1001/jamasurg.2017.0904.

[8] World Health Organization. Global guidelines for the prevention of surgical site infection. 2016. http://apps.who.int/iris/bitstream/handle/10665/250680/9789241549882-eng.pdf;jsessionid=1E47C47E25A5C6CBFB6F792009A84054?sequence=1.

[9] Frisch NB, Pepper AM, Jildeh TR, Shaw J, Guthrie T, Silverton C. Intraoperative hypothermia during surgical fixation of hip fractures. Orthopedics. 2016;39:e1170–e1177. doi:10.3928/01477447-20160811-04.

[10] Frisch NB, Pepper AM, Rooney E, Silverton C. Intraoperative hypothermia in total hip and knee arthroplasty. Orthopedics. 2017;40:56–63. doi:10.3928/01477447-20161017-04.

[11] Schmied H, Kurz A, Sessler DI, Kozek S, Reiter A. Mild hypothermia increases blood loss and transfusion requirements during total hip arthroplasty. Lancet. 1996;347:289–292.

[12] Rohrer MJ, Natale AM. Effect of hypothermia on the coagulation cascade. Crit Care Med. 1992;20:1402–1405.

[13] Allen MW, Jacofsky DJ. Normothermia in arthroplasty. J Arthroplasty. 2017;32:2307–2314. doi:10.1016/j.arth.2017.01.005.

[14] Legg AJ, Hamer AJ. Forced-air patient warming blankets disrupt unidirectional airflow. Bone Joint J. 2013;95-B:407–410. doi:10.1302/0301-620X.95B3.29121.

[15] McGovern PD, Albrecht M, Belani KG, Nachtsheim C, Partington PF, Carluke I, et al. Forced-air warming and ultra-clean ventilation do not mix: an investigation of theatre ventilation, patient warming and joint replacement infection in orthopaedics. J Bone Joint Surg Br. 2011;93:1537–1544. doi:10.1302/0301-620X.93B11.27124.

[16] Sharp RJ, Chesworth T, Fern ED. Do warming blankets increase bacterial counts in the operating field in a laminar-flow theatre? J Bone Joint Surg Br. 2002;84:486–488.

[17] Shirozu K, Kai T, Setoguchi H, Ayagaki N, Hoka S. Effects of forced air warming on airflow around the operating table. Anesthesiology. 2018;128:79–84. doi:10.1097/ALN.0000000000001929.

EXHIBIT DX3

TO DECLARATION OF BENJAMIN W. HULSE IN SUPPORT OF DEFENDANTS' MOTION FOR RECONSIDERATION OF THE COURT'S DECEMBER 13, 2017 ORDER ON GENERAL CAUSATION

UNITED STATES DISTRICT COURT

DISTRICT OF MINNESOTA

In re Bair Hugger Forced Air Warming Products Liability Litigation	MDL No. 15-2666 (JNE/FLN)
This Document Relates to All Actions	**EXPERT REPORT OF** **SAID ELGHOBASHI, M.SC., PH.D., D.SC.**

Attached as exhibit 1 is my report, Effect of Heated-Air Blanket on the Dispersion of Squames in an Operating Room, Dated March 23, 2017

Attached as exhibit 2 is a Summary of Opinions.

Attached as exhibit 3 is my professional Resume.

I have not previously testified in trial or deposition.

My hourly charge for professional services is $800.00

Date: March 29, 2017

A Elghobashi

Said Elghobashi, M.Sc., Ph.D., D.Sc.

Exhibit 1

Effect of Heated-Air Blanket on the Dispersion of Squames in an Operating Room

Said Elghobashi

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March 23, 2017

Contents

Effect of Heated-Air Blanket on the Dispersion of Squames in an Operating Room

Abstract

A large-eddy simulation (LES) of the interaction between the ventilation air flow and forced hot air from a blower is performed to investigate the effect of hot air on dispersion of squames in a realistic operating room (OR) consisting of an operating table (OT), side tables, surgical lamps, medical staff, and a patient. Two cases with blower-off and blower-on are calculated together with Lagrangian trajectories of 3 million squames initially placed on the floor surrounding the OT. The squames particles are assumed as spheres of size 10 microns and the drag, lift and buoyancy forces are considered in calculating their instantaneous motion. It is shown that with the blower-off, squames are quickly transported by the ventilation air away from the table and towards the exit grilles. However, with the hot air blower turned on, the ventilation air flow above and below the OT is disrupted significantly. The rising thermal plumes from the hot blower air drag the squames above the OT and the side tables and then they are blown downwards toward the surgical site by the ventilation air from the ceiling. Temporal history of number of squames particles reaching four imaginary boxes surrounding the side tables, the OT, and the patient's knee shows that several particles reach these boxes with the blower turned on. The study shows that LES is necessary to accurately capture the mixing and transport in a turbulent flow and predict the dispersion of squames in an OR.

1 Introduction

Microbial skin colonizers, such as *Staphylococcus aureus*, have been known as a major cause of surgical site infections in operating rooms (Noble, 1975; Clark & de Calcina-Goff, 2009; Wood *et al.*, 2014). These bacteria typically colonize on human skin cells or squames which are routinely shed by humans, roughly about 10^7 particles per day (Noble, 1975). The squame particle size ranges over 4–20 μm of equivalent diameter (Noble *et al.*, 1963; Lees & Brighton, 1972).

Reduction of post-operative surgical site infections has been linked to two main factors: (i) ultra-clean ventilation (UCV) systems, and (ii) perioperative patient warming (Ng *et al.*, 2006; Legg *et al.*, 2012; Wood *et al.*, 2014). Ultra-clean ventilation aims to reduce the quantity of airborne bacteria in the operating room (OR) and most importantly near the surgical site. This is typically achieved by the constant delivery of highly filtered ultra-clean air with a downward uniform velocity of 0.3-0.5 m/s (McGovern *et al.*, 2011). The UCV performance depends critically on volumetric airflow, proper temperature gradients, use of uniform downward flowing ventilation air, potentially in the laminar regime (Memarzadeh & Manning, 2002; Pereira & Tribess, 2005). Surgeons and other medical equipment within the operating room (surgical lights, tables, patient, computers, etc.), motion of surgeon's arms and their bending motion (Chow & Wang, 2012) can disrupt this air flow

and create wakes, flow unsteadiness, and turbulence, thereby increasing the amount of cfu in the OR.

Perioperative patient warming is the other important clinical practice to prevent inadvertent surgical hypothermia, wherein the core temperature of the patient drops below 36°C. Preventing inadvertent perioperative hypothermia has several benefits that include reduced operative blood loss, reduced duration of surgery, improved wound healing, reduced wound infections, reduction in postoperative ulcers, reduced duration of hospital stay, and increased survival rates (Wood *et al.*, 2014; Ng *et al.*, 2006; Legg *et al.*, 2012). Monitoring and maintaining body temperature during surgery is therefore an accepted and required practice. Warttig *et al.* (2014) review different methods used to combat inadvertent perioperative hypothermia. These include use of warm cotton blankets, reflective blankets, warmed intravenous and irrigation solutions, circulating warm water mattresses, a reusable electric blanket, an electric heating pad, and forced-air warmers (Kellam *et al.*, 2013; Austin, 2015). Of these, active warming using forced air warming (FAW) devices, and passive warming based on the use of reflective blankets, are the two main techniques used to keep the patient's body warm and prevent hypothermia. Although passive heating techniques may show similar effectiveness as the FAW devices, the latter have been used for over two decades due to their efficacy in maintaining patient's core body temperature. These techniques use forced convection to increase the skin temperature and the total body heat content. These devices contain a blower (such as 3M™ Bair Hugger™) that extracts the room temperature air through an air-intake filter heats the air using a heating coil, and vents the air into the sterile field adjacent to the operative site (Albrecht *et al.*, 2011; Leaper *et al.*, 2009; Wood *et al.*, 2014). The filtered and warm air flows through a connecting hose into blankets made of plastic and exits the blankets through tiny holes over the patient's skin. However, this forced warm air has the potential to generate and mobilize airborne contamination in the operating room.

A number of studies have examined at the safety of forced-air warming, and whether FAWs can affect surgical site infections through mobilized airborne contamination. FAWs can potentially lead to surgical site contamination in two ways: (i) direct contamination of the air from the blowers that reaches the patient's body, and (ii) disruption of the ultra-clean ventilation air by the thermal plumes and turbulence. The former risk can potentially be reduced by using intake filers that are HEPA-rated and show high filtration efficiency. The latter has been studied extensively as reviewed

by Wood *et al.* (2014). It is hypothesized that the temperature gradients and resultant thermal plumes created by the FAW devices could disrupt the benefits of UCV flow, that is designed to be uniform and downwards. The interaction between the FAW and UCV flows may lead to increased surgical site infections (SSI).

McGovern *et al.* (2011); Legg *et al.* (2012) have shown that temperature gradients and excess heat created by FAW devices can transport air from the unsterilized floor level to the surgical site, thus increasing the potential risk of SSIs. Moretti *et al.* (2009) measured an increase in the bacterial load when FAWs were used. Lack of flow visualization is the main drawback of these studies as it does not provide information about whether the particles came from the floor or from the FAW blower. Legg *et al.* (2012); Sessler *et al.* (2011) used smoke particle visualization to understand the source of these particles near the surgical site comparing cases with no warming, FAW, and radiant warming. Although they found that FAW increased the particle count with blower turned on (almost 10-fold increase), they also showed that the uniform, laminar flow from the ultra-clean ventilation reduced the effect of particles by limiting their numbers near the surgical site.

It is clear from the available literature that the interaction between the UCV flow and the rising plumes from the forced-air warming devices plays a critical role in deciding whether FAWs indeed can lead to increased number of particles near the surgical site. However, there have not been detailed experimental measurements of flow patterns in the OR setting with the FAW blower turned on. Recently, McNeill *et al.* (2012, 2013) conducted particle-image velocimetry (PIV) measurements to understand the flow pattern in an OR with the ultra-clean ventilation system. This study, however, did not investigate the effect of FAW blower. McNeill *et al.* (2013) also made detailed measurements of temperature fields on surgeon's and patient's body to be used for computational modeling. Although the above PIV was able to visualize and measure the flow field, it was limited to planar data (2D PIV) and thus a full three-dimensional data are not available for the OR. Nevertheless, some useful information on the flow unsteadiness, turbulence within the room was obtained from the McNeill *et al.* (2013) study.

The only other way to characterize the flow field in an OR with and without FAW blowers, is to use computational fluid dynamics (CFD) modeling in three-dimensions. This, however, is a difficult task due to the size and complexity of the domain involving medical equipment, staff, computers, etc. There are only few CFD studies in the literature that used Reynolds-averaged Navier

Stokes (RANS) models (Memarzadeh & Manning, 2002; Memarzadeh, 2003; Chow & Wang, 2012), wherein only the time-averaged velocity field is computed. All information about the turbulence and velocity fluctuations is completely *modeled*. As is shown later (section 3), RANS approach is not predictive, since the instantaneous velocity field needed for calculating the trajectories of squames is not directly computed. Thus, RANS is incapable of accurately predicting the locations of squames at any time in the OR. Memarzadeh & Manning (2002); Memarzadeh (2003) investigated the effect of various UCV inlet flow conditions on the transport of squames particles in an OR. They considered a realistic OR with medical staff, equipment, surgical lamps, etc. and accounted for the thermal plumes created by heat radiated from various sources. However, they used a RANS model coupled with a Lagrangian particle-tracking of around 4000 representative particles. Their study did not include the FAW blower discharge. They showed that use of a uniform inlet flow with laminar conditions[1] is better for reducing the number of particles near the surgical site. In addition, they found that the thermal plume created by the hot surface of the surgical site prevented particles from reaching the site. They showed that roughly 2-5% of particles reach the surgical site, *provided they are originated very close, about* 1.3cm *above the site*. Particles originating from locations away from the surgery did not have a statistically significant probability of reaching the surgical site. As is discussed later in section 3, RANS model cannot compute the instantaneous velocity field needed to accurately calculate the forces on particles, and particle trajectories.

Chow & Wang (2012) investigated the ultra-clean ventilation flow and its effect on bacteria-carrying particles in an OR using a RANS model as well. They simulated the bacteria particles as a non-inertial pollutant, wherein an Eulerian transport equation for the concentration of the bacteria is calculated. In addition, they considered periodic bending movement of one of the surgeons performing the operation. They found that if the surgical staff stands upright (no bending), the UCV flow keeps the bacteria concentration very low (< 1 cfu/m^3) near the surgical site. However, with the surgeon's bending motion included, they showed that this concentration increased to larger than the recommended value (10 cfu/m^3).

All of the above computational studies are based on RANS modeling and did not include the

[1] It should be noted that the literature uses the terminology 'laminar flow' for the ultra-clean ventilation flow. Based on the standard values of air changes per hour (ACH) for an OR (25 per hour), the inlet grille sizes, and properties of air, the flow Reynolds numbers are much larger than 2000, a critical value beyond which turbulence occurs in a duct. The inlet grille flow, thus is not typically laminar. Although the level of turbulence in the inlet flow is not large ($< 10\%$), the flow contains velocity fluctuations and is unsteady.

FAW blower system together with a blanket cover above the patient. In order to assess the interaction between UCV and FAW blower, a systematic, predictive simulation is needed. Large-eddy simulation (LES) is a numerical technique that involves computing the properties of the large, energy-containing eddies of turbulence accurately, without any user adjustable tuning parameters, and models only the more homogeneous, small scales of turbulence (Pope, 2000; Piomelli, 2014). This technique provides the instantaneous three-dimensional velocity, temperature, and pressure fields and has been shown to be far more accurate than the RANS model. Section 3 outlines the differences between LES and RANS in detail. In addition, since the time dependent, three-dimensional velocity field is available in LES, then the forces on particles and their trajectories can be calculated accurately (Apte *et al.*, 2003*b*; Ham *et al.*, 2003; Apte *et al.*, 2009; Moin & Apte, 2006; Mahesh *et al.*, 2006). The only challenge with this technique is that it is computationally intensive and requires fine grid resolutions and small time-steps to capture the large-scales of turbulence. Recent advances made in algorithmic developments for LES on arbitrary shaped, unstructured grids (Mahesh *et al.*, 2004; Ham *et al.*, 2003; Moin & Apte, 2006; Mahesh *et al.*, 2006; Ham & Iaccarino, 2004) have facilitated application of LES to more realistic problems involving complex geometries and flow conditions. These advances have been successfully applied to turbulent, reacting flows in a gas-turbine combustion chamber and has led the gas-turbine industry to switch from RANS to the predictive LES technique in their design cycle (Moin & Apte, 2006; Mahesh *et al.*, 2006; Apte *et al.*, 2009).

LES applied to operating rooms with medical staff and other instruments is still challenging, owing to the size of the room and the complexity of the geometries involved. At the time of writing this report, only one LES study has been performed for an operating room by Saarinen *et al.* (2015). They studied the escape of air into an isolation room during opening and closing of a door and passage of a human figure. They used passive smoke visualizations to compute the volume flux of air when a door is opened. Although this study had some complex geometry (a human figure), it did not have the intricacies of the OR table, surgeons, patient and other medical equipment, nor it computer the dispersion of squames in the OR. Nevertheless, it showed that LES can accurately predict such flows through validation with experimental observations.

The main goal of the work reported here is to use large-eddy simulation to compute the interaction of the OR ultra-clean ventilation air flow and the flow created by forced air warming

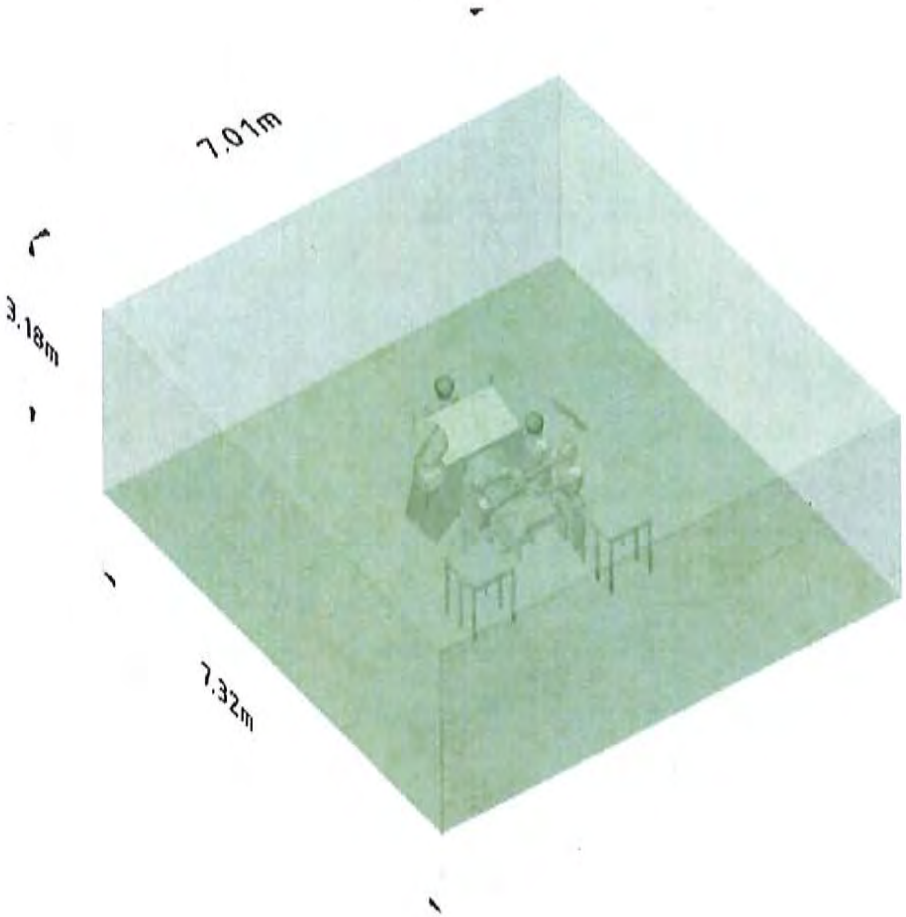
system (such as 3M™ Bair Hugger™) and investigate their impact on the dispersion of squames. Specifically, computations are conducted for the cases with blower-off and blower-on, including the Lagrangian tracking of inertial squame particles, starting from the operating room floor, to prove whether the FAW system and the resultant thermal plumes play a role in transporting squame particles to the surgical site.

The rest of the report is arranged as follows. In section 2, details of the operating room geometry and CAD model are described. This includes the OR dimensions, the surgical lamps, four medical staff, an operating room table, two side tables, the blower, and the patient undergoing knee surgery. The numerical approach is described in section 3. This includes a detailed discussion of LES and RANS, the governing equations used for LES, the computational grid, and the boundary conditions. The numerical algorithm used is briefly summarized in section 3.5. This is followed by detailed description of the results in section 4 on flow field, particle trajectories and particle counts that reach the surgical site and other key regions of interest. Finally, the findings are summarized in section 5.

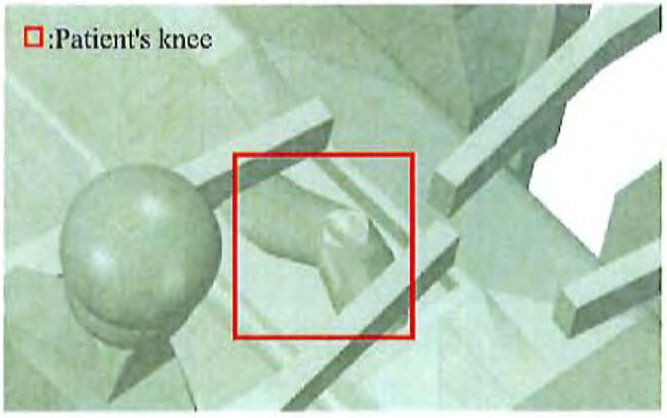
2 Operating Room Geometry and CAD Model

The operating room CAD (computer aided design) model was created using Ansys® SpaceClaim Direct Modeler™ (ANSYS, Inc., Canonsburg, PA, USA). The CAD model replicated a realistic operating room (OR) depicting a knee surgery being performed on a patient. An original baseline CAD model was obtained from M/E Engineering P.C. (Straub, 2016) and was further modified to incorporate the measured dimensions of the inlet air grilles and the surgical drape as shown below. Figure 1a shows the OR dimensions used to create the CAD model. The length, width and height of the room are 7.32m, 7.01m and 3.18m, respectively. These dimensions are from 3M video at: https://www.youtube.com/watch?v=QbzeInWIJ54. Figure 1b shows a close-up view of the surgeon's hands extended over the patient's knee mimicking a real world operating procedure.

The CAD model also includes several objects that are usually present in a real OR. Typically, there can be several combinations of such objects, but for this study the following objects were included in the model. These are shown in a top view in figure 2 and include: (i) OR Table; (ii) OR drape; (iii) patient's body under the drape with knee exposed; (iv) four surgeons (two of the surgeons have extended hands and two have hands down), (iv) two side tables, (v) two surgical lamps, (vi)



(a)



(b)

Figure 1: CAD model showing (a) operating room dimensions, and (b) closeup of the patient's knee.

3M™ Bair Hugger™ blower unit (partly visible near the top left corner under the drape).

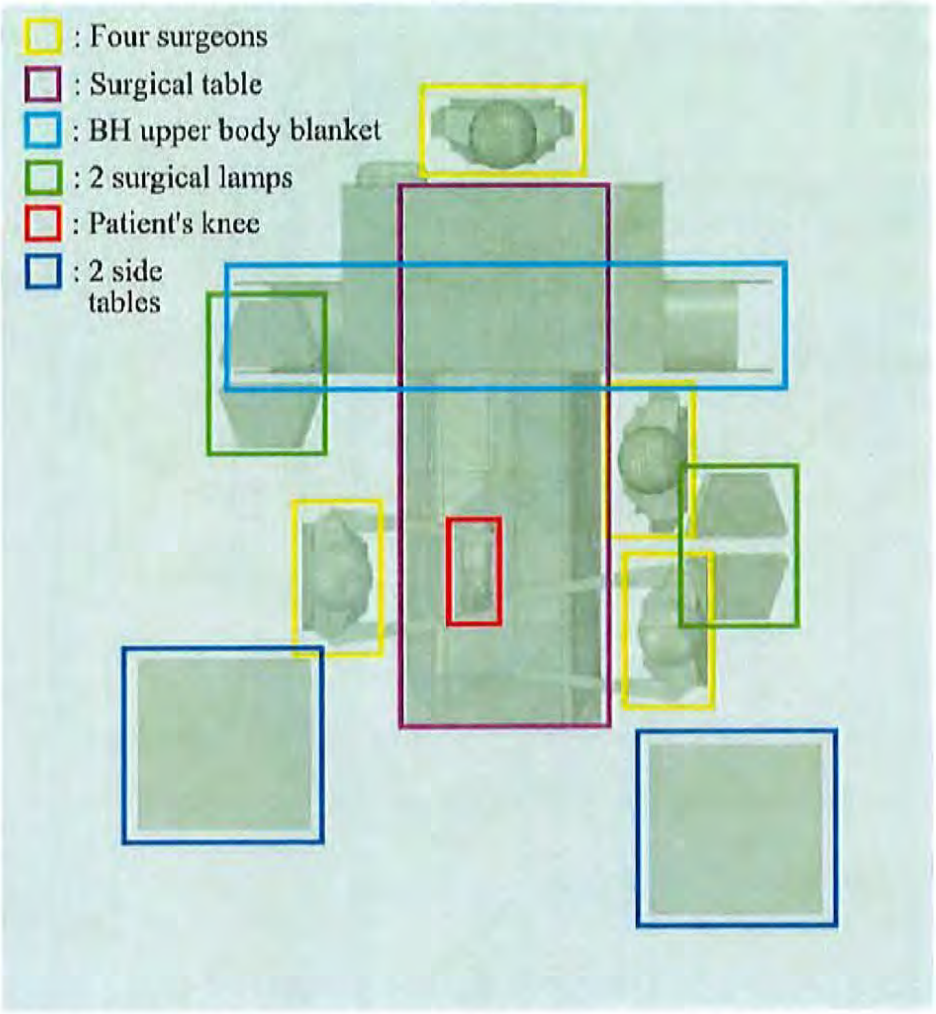


Figure 2: Close-up view of various objects included in the CAD model.

Figure 3 shows a side view of the OR table together with a few key dimensions. The bottom of the OR table is 0.94m above the floor of the room. The drape on the OR table covering the patient's torso is suspended 0.52m above the floor. The 3M™ Bair Hugger™ blower unit is also seen in the bottom right side of the figure.

The drape design from the base CAD model was modified to better represent the drape layout in a real OR room. The modifications mainly focused on using accurate dimensions and shape of the drape near the front end based on an actual picture taken in an OR room as shown in figure 4b. A corresponding CAD model used in the present study is shown in figure 4a. For the CAD model, the

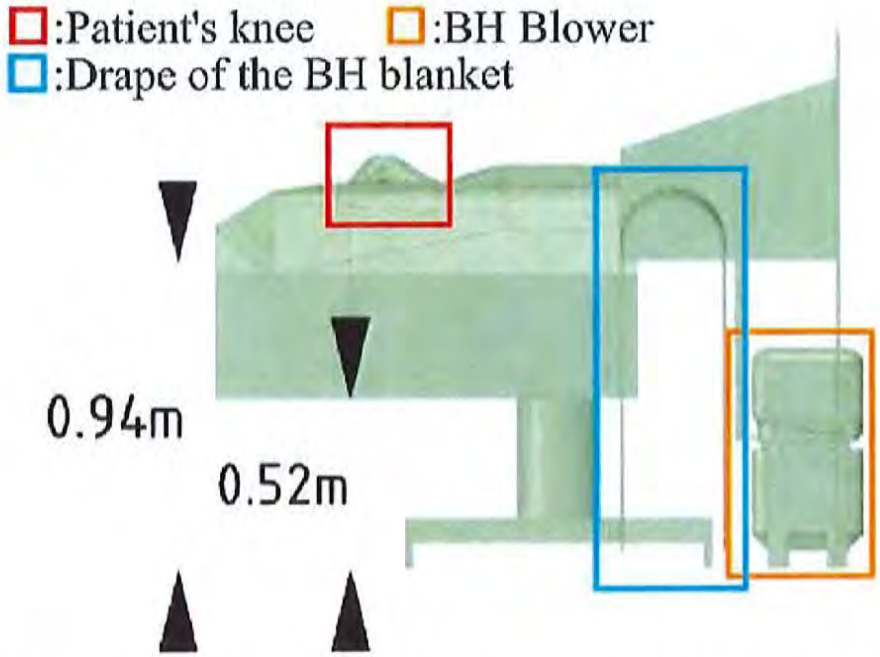


Figure 3: Side view of the OR table with some key dimensions. The 3M™ Bair Hugger™ blower unit is clearly visible on the bottom ride side.

front end of the drape was designed to mimic the shape obtained by dimensions A, D, C, E in figure 4a. The dimensions in the CAD model are given in both metric and imperial units (in brackets) in this figure to facilitate direct comparison with the real picture on the right. The distance between the vertical bars holding the drape, denoted by dimension F in Figure 4b, was also implemented in the CAD model.

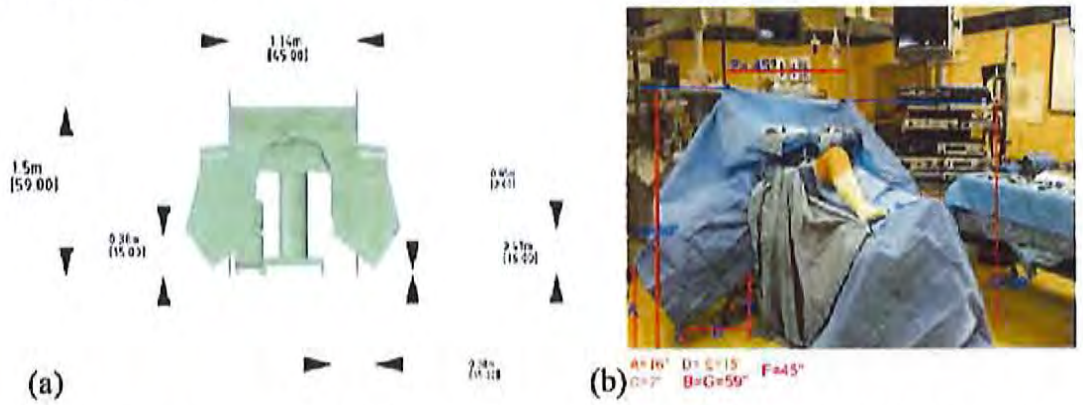


Figure 4: Drape dimensions and configuration: (a) model developed to match the drape dimensions, (b) actual drape picture in an OR room. The dimensions are shown in both metric and imperial units (in brackets).

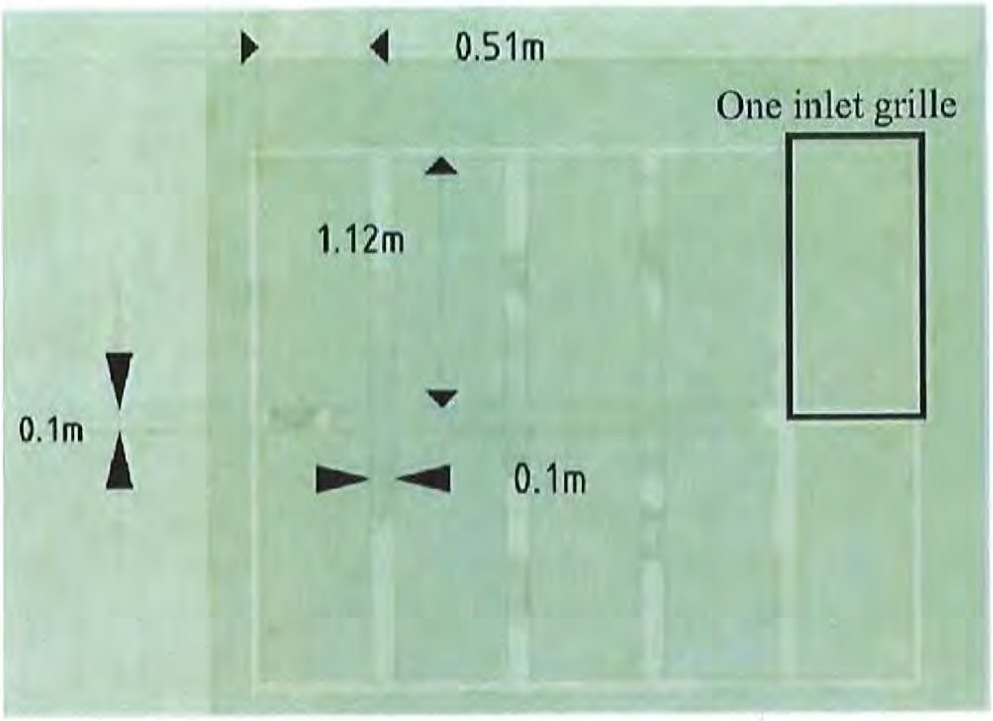


Figure 5: Ten inlet grills to supply clean filtered air into the OR.

The CAD model included ten inlet grilles (figure 5) for supplying clean filtered air to the OR. Each inlet grille is 0.51m in width and 1.12m in length. All ten grilles are of the same size. There is a gap of 0.1m between the neighboring grilles at all sides.

There are four exhaust (or outlet) vents, two on each side wall. Figure 6 shows two outlet grilles (with the other two outlets located on the opposite wall). Each outlet grille is 0.71m in width and 0.71m in length.

3 Numerical Simulation

A state-of-the art, fully parallel, unstructured, co-located grid flow solver based on principles of kinetic energy conservation for large-eddy simulation (Moin & Apte, 2006) of turbulent flow in the limit of zero-Mach numbers is used in this study. This solver is MPI-based, uses algebraic multigrid for the pressure Poisson equation, and third-order WENO-based scheme for transport of scalar fields such as temperature. It has been thoroughly validated for a number of different particle-laden turbulent flows (Apte *et al.*, 2003*b*,*a*, 2008*a*, 2009, 2008*b*) including swirling turbulent flow

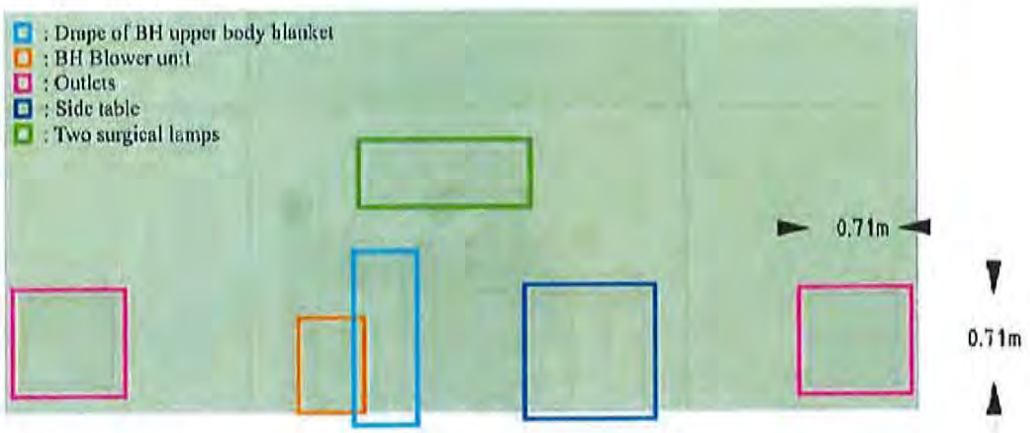


Figure 6: Outlet (exhaust) grilles for air exit from the room. Out of the four outlets in the CAD model, only two are visible in the picture. The other two outlets are on the the opposite wall.

in a co-axial combustor, turbulent reacting flow, as well as spray combustion in a realistic Pratt and Whitney gas-turbine combustion chamber (Moin & Apte, 2006; Mahesh *et al.*, 2006).

3.1 Large-eddy Simulation (LES): Introduction and Need

The physics of turbulent air flow containing heated buoyant plumes and laden with inertial particles in a real-life operating room is highly complex. Simulating such flows with predictive capability is difficult as turbulence, by nature, consists of a broad range of length- and time-scales and is inherently three-dimensional. In addition, the geometry of a realistic operating room consists of complex surfaces involving surgeons, operating table, surgical lights, patient, among other. If a probe measures the velocity at a certain location in such a flow, the velocity signal will show a broad range of frequencies and fluctuations around a mean. A typical kinetic energy spectrum obtained via Fourier transform of turbulent velocity field is shown in figure 7, especially for moderate to large Reynolds numbers. The spectrum is broad-band with large amount of kinetic energy per wavenumber present at large scales (small wavenumbers) and small amount of energy present at smaller scales (larger wavenumbers). There also exists an inertial range, scales in this regime simply transfer the energy from larger scales to smaller scales through a process commonly known as the energy cascade (Pope, 2000). As the Reynolds number increases, this spectrum is known to broaden. The largest scales ($\mathscr{L}$) of motion are typically confined by the size of the domain (for example, size of the inlet jet

or size of the room). However, as the Reynolds number increases, the smallest scales of motion (known as the Kolmogorov scales, η) are reduced until the kinetic energy is dissipated into internal energy by the viscous effects. Owing to this broad range of scales, prediction of turbulent flows at large Reynolds numbers becomes difficult and is only possible if the behavior of all scales of motion is captured properly.

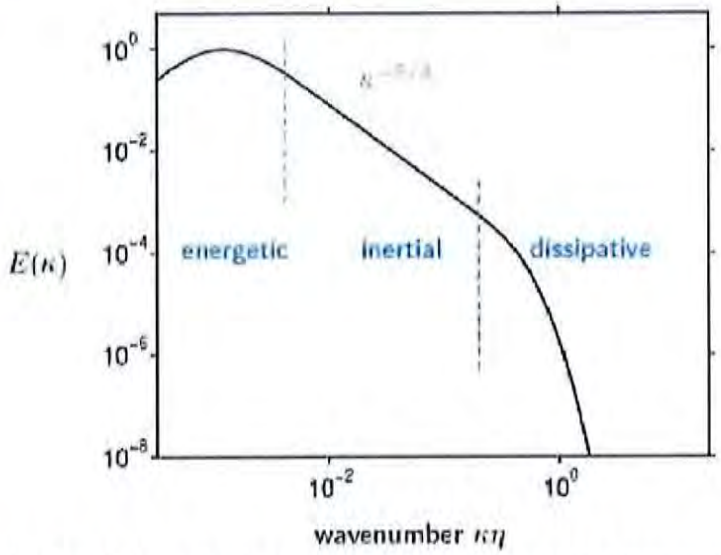


Figure 7: Schematic of a turbulence kinetic energy spectrum showing energy per wavenumber as a function of the wavenumber (Pope, 2000). The inertial range of scales is indicated by the -5/3 slope line that separates the energetic large scales and dissipative small scales of turbulence. In DNS, the grid resolution is fine enough to capture all scales, whereas in LES, the grid resolution is coarser (typically 10 times the Kolmogorov length scale), placing the grid cut-off somewhere in the inertial range.

Three basic approaches can be identified for prediction of turbulent flows: (i) direct numerical simulation (DNS), (ii) Reynolds averaged Navier-Stokes (RANS) modeling, and (iii) large-eddy simulation (LES), and are briefly described below.

DNS: In direct numerical simulation (DNS), the Navier-Stokes equations are solved on a computational grid that is fine enough, in space and time, to directly capture *all* the scales associated with the fluid flow motion without requiring any additional models. This means that the computational grid in three-dimensions is small enough to capture the smallest scales of turbulence and the time-step is small enough to capture the smallest time-scale associated with the flow. Using scaling arguments based on the Kolmogorov hypotheses (Tennekes & Lumley, 1972; Pope, 2000) used in the theory of turbulence, it can be shown that for a simple homogeneous, isotropic turbulence in a box, the grid resolution requirement ($\Delta \sim \mathscr{L}/\eta$; where $\mathscr{L}$ is the size of the large, energy-containing

eddies) for DNS varies as $Re_{\mathscr{L}}^{3/4}$, where $Re_{\mathscr{L}}$ is the Reynolds number based on $\mathscr{L}$ and the velocity fluctuations u, in one coordinate. Hence, the total number of mesh points needed in three-dimensions varies as $Re_{\mathscr{L}}^{9/4}$. A simple isotropic turbulence in a box at $Re_{\mathscr{L}} = 2000$, would require computational grid containing about 27M control volumes ($= 300^3$). In addition, based on numerical constraints of a computational solver, for a fluid flow of unit velocity, the grid spacings (Δ) and the time-steps (Δt) are roughly of the same order of magnitude ($CFL = u\Delta t/\Delta \sim 1$) and thus the spatio-temporal resolution will require a computational power that increases as $Re_{\mathscr{L}}^3$. Owing to the grid requirements and associated computational costs, DNS is not practical for realistic engineering applications and is restricted to canonical geometries and flow problems to study the fundamentals of turbulence (Moin & Mahesh, 1998).

RANS: According to the above discussion, the computation of practical turbulent flows relies predominantly on the Reynolds-averaged Navier-Stokes (RANS) equations approach. In RANS, the governing equations are averaged in time to obtain equations for the *time-averaged* velocity field, $\overline{u}(\mathbf{x})$. Thus, in this approach, only the mean velocity field that varies in space is obtained, and all information about the time-dependent fluctuations of the velocity field around the mean flow is lost. Because the momentum equations are non-linear (owing to the inertial, advective terms), a time-average of the non-linear term creates additional quantities that are unknown, giving rise to the classical closure problem of turbulence (Tennekes & Lumley, 1972; Pope, 2000). In order to evaluate these terms, models are introduced wherein the effect of the entire spectrum of turbulence (involving the large, inertial, and small scales shown in Figure 7) is completely modeled. This is usually done by introducing two additional transport equations for the turbulence kinetic energy (k) and the kinetic energy dissipation rate (ε), giving rise to the $k-\varepsilon$ model. It should be noted that the transport equations for k and ε also contain a large number of unknown, unclosed terms which also need to be modeled. The model constants are obtained by fitting the RANS predictions to the experimental data on simple, canonical flows such as wall bounded channel flow, isotropic turbulence, or free-shear flows. Because these models and model constants *are not universal*, using them for a complex flow such as air circulation in an operating room, invariably provides inaccurate results. Experimental data is necessary to adjust the model constants and thus the RANS models are not *predictive*. However, since only the time-averaged velocity field is calculated, the RANS approach is computationally the least expensive because it does not require the spatio-temporal resolution

necessary for the DNS studies. There are modified approaches, wherein the large-time scale variations are captured by solving the RANS equations in an unsteady manner. These unsteady-RANS simulations also suffer from the same hypotheses and models used for the basic RANS and their predictive capability is also poor.

LES: The energy spectrum (figure 7) shows that a substantial portion of the turbulence kinetic energy (TKE) is contained in the large-scales, known as the energy containing scales. In LES, only the contribution of the large, energetic structures to momentum and energy transfer is computed exactly, and the effect of the small scales, also termed as unresolved or subgrid scales, of turbulence is modeled. Since the small scales tend to be more homogeneous, and less affected by the domain boundary conditions as compared to the large eddies, then the subgrid closure models used in LES are universal and can be applied to a range of flows as compared to the RANS closures. Owing to these differences between the LES and RANS approaches, LES has been shown to be far superior to RANS in accurately predicting turbulent mixing of momentum and scalar (Mahesh *et al.*, 2004), pollutant and heat transport, combustion (Pierce, 2001)), and particle dispersion (Apte *et al.*, 2003*b*; Ham *et al.*, 2003).

In LES, the Navier-Stokes (NS) equations are filtered in space (as opposed to time as done in RANS) using a local filter (Gaussian, box, spectral etc.) to obtain a filtered velocity field, $\overline{u}_i(\mathbf{x}, t)$ (Pope, 2000). Using the local grid resolution as a spatial filter, the small, under-resolved scales of turbulence are filtered out. However, applying the filtering operation to the inertial, non-linear terms in the NS equations, gives rise to the closure problem. The resulting additional terms need to be modeled. Most often, the models used to close the unknown terms, known as Reynolds stresses, are based on the same types of assumptions, such as the gradient diffusion hypothesis, as employed in RANS. However, the fact that, in LES, modeling is only applied to capture the effect of unresolved, subgrid scales, which are homogeneous and universal, the closure models work very well in a wide range of problems. A dynamic procedure, typically employed in LES subgrid scale modeling, renders the modeling process completely free of any tuning parameters in contrast to RANS. All constants in the model are obtained directly in the calculations and are not set by the user. As long as the grid resolution is sufficient such that the motion of the energy-containing large eddies is captured correctly, unlike RANS, the LES approach can then be used in a truly predictive manner.

In addition, away from the boundaries, a typical LES grid can be 10 times coarser than a DNS grid in each direction (that is 10 times the Kolmogorov scale), resulting in significant savings in the computational cost. This makes LES an attractive tool compared to the DNS. However, there are still several challenges. Just like DNS, the LES computations are inherently three-dimensional and time-dependent, making the cost of the calculation large as the important large-scale spatio-temporal variations in the flow must still be resolved. In addition, the computational algorithm must not add large amounts of numerical dissipation as it has been shown that dissipative numerical approaches mask the physical dissipation present in turbulent flows and provide inaccurate predictions (Mittal & Moin, 1997; Kravchenko & Moin, 1997). These restrictions typically limits the use of LES to simple, canonical geometries and flows (as free-shear flows (jets, wakes, shear layers), wall bounded channel flows, or flow over backward facing step (Pierce, 2001; Piomelli, 2014)) for which the underlying algorithms are based on a non-dissipative schemes developed for structured Cartesian grids.

Applying LES to the complex and realistic geometries of engineering applications such as the the operating room; including the operating table, surgeons, patient and other equipment, or other applications such as gas-turbine combustors, propellers, among others, requires use of arbitrary shaped unstructured meshes. In recent years; however, considerable progress has been made in handling complex configurations and unstructured grids accurately (Piomelli, 2014). Mahesh *et al.* (2004); Ham *et al.* (2003); Mahesh *et al.* (2006) have developed a numerical algorithm for high-fidelity simulations of incompressible, variable density flows on unstructured grids. A novelty of their algorithm is that it is discretely energy-conserving which makes it robust at high Reynolds numbers *without numerical dissipation*. This makes LES applicable to complex configurations and it has been successfully used to simulate multiphase, spray combustion processes in a realistic Pratt and Whitney gas-turbine combustion chamber (Moin & Apte, 2006; Mahesh *et al.*, 2006; Apte *et al.*, 2009). These simulations are still computationally intensive, often requiring 3–4 weeks of simulation on parallel supercomputers, however, the detailed data obtained from the simulations are of significant importance to researchers and engineers since such information could not be obtained from laboratory experiments. This has led several gas-turbine industries, who generally use RANS in their design cycle, to switch from RANS-based approaches to LES.

Furthermore, turbulent flows laden with dispersed particles (either solid particles, or droplets or

bubbles) involve the complexity of capturing the dynamics of turbulence as well as that of the dispersed phase. The physics of particle-turbulence interactions is complex (Elghobashi, 1994, 2006), and depending upon the magnitudes of the particle relaxation times relative to the Kolmogorov time scales, heavier-than-fluid particles (solid particles, droplets, squames) can exhibit behavior such as preferential clustering on the edges of vortices (Eaton & Fessler, 1994; Rouson & Eaton, 2001; Kulick *et al.*, 2006; Reade & Collins, 2000; Eaton & Segura, 2006), whereas, lighter-than-fluid particles (bubbles) can break the vortical structures (Ferrante & Elghobashi, 2004; Druzhinin & Elghobashi, 1998; Ferrante & Elghobashi, 2007; Sridhar & Katz, 1999).

RANS is not capable of capturing this complex physics of particles interacting with turbulence because only the mean velocity field is computed by RANS, yet it is commonly used owing to its low cost. However, if the objective is to accurately simulate the dispersion of inertial particles in a turbulent flow, then a three-dimensional, instantaneous velocity field is necessary to calculate the forces on the particles. Inertial particle trajectories and dispersion are strongly influenced by the spatio-temporal variations in the velocity fields. Hence, using only the mean velocity field provides inaccurate dispersion characteristics. An improved RANS to capture the transient effects uses a model for particle motion that utilizes the local turbulence kinetic energy and introduces some randomness (typically a Gaussian distribution) in the particle equations (Sommerfeld *et al*., 1992) is necessary. Recent work on the dispersion of squames in an operating room and the effect of different inlet air flow conditions used RANS together with such a stochastic, Lagrangian particle-tracking algorithm (Memarzadeh & Manning, 2002). Such a model must be tuned by the user to calculate different particle-laden flows and can behave differently in free-shear versus wall-bounded flows. As can be seen from the results presented by Sommerfeld *et al.* (1992); Chen & Pereira (1998), particle dispersion predicted using a RANS approach for turbulent flows in a wide range of applications involving swirling, separated flows do not agree with the experimental data. However, the same flowfields computed using LES (Apte *et al.*, 2003*b*; Moin & Apte, 2006; Apte *et al.*, 2008*b*, 2009) show considerably better predictive capability and agree with the experimental data very well. In LES, the resolved instantaneous velocity field, which varies in time and space, at the particle location is used to compute the forces on the particles as opposed to the time-averaged velocity in RANS. Accordingly, the effect of the energetic, turbulence scales (of the order of the grid resolution and larger) are completely captured in LES, thus predicting its impact on particle dispersion directly.

To summarize, it is essential to use LES instead of RANS to accurately predict the air circulation and dispersion of squames in an operating room for the following reasons:

- LES provides a three-dimensional, instantaneous flow field (velocity, pressure, temperature) of the resolved, energetic, large-scales, and only models the effect of the unresolved, subgrid (small) scales of turbulence. The subgrid scales tend to be more homogeneous, and less affected by the domain boundary conditions and thus allow the appropriate use of the eddy-viscosity models to calculate their stresses. RANS, on the other hand, only calculates the time-averaged velocity field and models the effect of all the scales of turbulence on the mean flow, resulting in unrealistic flow predictions.

- The subgrid model constants used in LES can be obtained dynamically, thus making LES truly predictive without any user-defined tuning parameters, whereas RANS model constants are not universal and often require manual tuning.

- LES is considerably more accurate in predicting passive as well as inertial particle dispersion since the instantaneous, three-dimensional resolved velocity field is available for computing the forces on the particles. In RANS, a random perturbation must be added to the mean velocity field to construct an artificial, time-dependent, three-dimensional velocity field needed to calculate the particle motion. This renders the calculation of particle dispersion highly inaccurate.

3.2 Governing Equations

The air flow in an operating room involves temperature variations within the room owing to various sources of heat; such as the operating room lamps, heat radiated from the medical personnel bodies, hot air discharged from a blower system, among others. The local temperature variations change the local air density. However, since the air flow in the room is low-speed (maximum velocity on the order of, $u \sim 0.5$ m/s compared to speed of sound of around, $c \sim 343$ m/s), the Mach number (u/c), that represents the ratio of acoustic to convective time-scales, is small ($<< 0.01$). Small Mach numbers mean that the convective time-scales are much larger than acoustic time-scales, and thus the compressibility effects are negligibly small. Under these conditions, the variable-density equations in the limit of zero-Mach number are valid and the pressure field at any point within the

domain and time can be split into a bulk thermodynamic pressure, P_0, and the dynamic pressure p that appears in the momentum equation,

$$P(x,t) = P_0(t) + p(x,t). \tag{1}$$

The background thermodynamic pressure (P_0) for the operating room is assumed constant and equal to the atmospheric pressure, $P_0 = 1$ atm.. Accordingly, the density of the air (assumed as ideal gas) varies only with the local temperature field according to the equation of state as,

$$\rho = \frac{P_0 R_{\text{universal}} T}{M_{\text{air}}}, \tag{2}$$

where $R_{\text{universal}}$ is the universal gas constant, M_{air} is the molecular mass of the air, and T is the absolute temperature. The governing equations for large-eddy simulation of turbulent flows with variable density in the limit of zero Mach number are given below.

3.2.1 Gas-phase equations

The spatially filtered, Favre averaged, governing equations used for large-eddy simulation of particle-laden, turbulent air flow with heat transfer and buoyancy effects are given as,

$$\frac{\partial \overline{\rho_g}}{\partial t} + \frac{\partial \overline{\rho_g} \tilde{u_j}}{\partial x_j} = 0. \tag{3}$$

$$\frac{\partial \overline{\rho_g} \tilde{u_i}}{\partial t} + \frac{\partial \overline{\rho_g} \tilde{u_i} \tilde{u_j}}{\partial x_j} = -\frac{\partial \overline{p}}{\partial x_i} + \frac{\partial}{\partial x_j}\left(2\overline{\mu}\tilde{S_{ij}}\right) - \frac{\partial q_{ij}^r}{\partial x_j} + (\overline{\rho_g} - \rho_0) g_i, \tag{4}$$

$$\frac{\partial \overline{\rho_g} \tilde{h}}{\partial t} + \frac{\partial \overline{\rho_g} \tilde{h} \tilde{u_j}}{\partial x_j} = \frac{\partial}{\partial x_j}\left(\overline{\rho_g}\tilde{\alpha_h}\frac{\partial \tilde{h}}{\partial x_j}\right) - \frac{\partial q_{hj}^r}{\partial x_j}, \tag{5}$$

where

$$\tilde{S_{ij}} = \frac{1}{2}\left(\frac{\partial \tilde{u_i}}{\partial x_j} + \frac{\partial \tilde{u_j}}{\partial x_i}\right) - \frac{1}{3}\delta_{ij}\frac{\partial \tilde{u_k}}{\partial x_k}. \tag{6}$$

Here, $\overline{\rho_g}$ is the filtered density, $\tilde{u_i}$ is the Favre averaged velocity field, $\overline{p}$ is the filtered pressure, μ is the dynamic viscosity, $\alpha_h = k/\overline{\rho}_g C_p$, is the thermal diffusivity (k is the conductivity and C_p the specific heat at constant pressure), g_i is the gravitational acceleration, and $\tilde{S_{ij}}$ is the filtered rate of

strain. In addition, the specific enthalpy, h, is given as,

$$h = \frac{T - T_0}{T_0}, \tag{7}$$

where T is the local temperature. Also, T_0 and ρ_0 are the temperature and density fields corresponding to the air inlet conditions and pressure of P_0.

The additional terms q^r_{ij} and q^r_{hj} in the momentum and the enthalpy equations, respectively, represent the subgrid-scale stress and energy flux and are modeled using the dynamic Smagorinsky model by Moin *et al.* (1991) as demonstrated by Pierce & Moin (1998*a*). The unclosed terms in Eqs. (4-5) are modeled using the gradient-diffusion hypothesis with eddy-viscosity/diffusivity,

$$q^r_{ij} = \overline{\rho_g}(\widetilde{u_i u_j} - \tilde{u}_i \tilde{u}_j) = 2\mu_t \tilde{S}_{ij} - \frac{1}{3}\overline{\rho_g} q^2 \delta_{ij}, \tag{8}$$

$$q^r_{hj} = \overline{\rho_g}(\widetilde{h u_j} - \tilde{h}\tilde{u}_j) = \overline{\rho_g}\alpha_t \frac{\partial \tilde{h}}{\partial x_j}, \tag{9}$$

where the eddy viscosity (μ_t) and eddy thermal diffusivity α_t are modeled as,

$$\mu_t = C_\mu \overline{\rho_g} \overline{\Delta}^2 \sqrt{\widetilde{S_{ij}}\widetilde{S_{ij}}}, \tag{10}$$

$$\overline{\rho_g}\alpha_t = C_\alpha \overline{\rho_g} \overline{\Delta}^2 \sqrt{\widetilde{S_{ij}}\widetilde{S_{ij}}}. \tag{11}$$

The coefficients C_μ, C_α are calculated dynamically at each time-step and for each grid point using the dynamic procedure as outlined by Germano *et al.* (1991). For the unstructured grids, the filter width $\overline{\Delta}$ is taken as $V_{cv}^{1/3}$ where V_{cv} is the volume of the grid element.

3.2.2 Equations for calculating the trajectories of individual squames

The human skin cells or squames typically are disc-shaped with a diameter ranging from 4–20μm and a thickness of 3–5μm with density close to that of liquid water (1000kg/m^3) (Noble *et al.*, 1963; Noble, 1975; Snyder, 2009). Although the squames shape is more disc-like, in the present work they are considered as non-deformable, spherical in shape. A spherical shape is assumed as the dynamics of the spherical particle is easier to calculate and also the lift and drag forces on small particles of disc or spherical shape are not significantly different. The diameter of the spherical

particle is assumed to be 10 microns and matches an average settling velocity of a disc-shaped particle considering the mean flow normal and parallel to the disc (see Appendix A). Recent work using RANS model by Memarzadeh & Manning (2002); Memarzadeh (2003) also approximates the squames particles as spherical with a size of 10 microns.

An Eulerian-Lagrangian approach is used wherein individual squames trajectories will be tracked in a Lagrangian frame. The different forces on the particles will be calculated using standard closure laws. The effect of the particles on the fluid flow will be negligible owing to their small concentration and thus a one-way coupling approach is adopted, wherein the squame motion uses the fluid flow parameters (velocity) to compute the forces, however, the effect of squames on the fluid momentum is neglected (Elghobashi, 1994, 2006). In addition, since the volume fraction of the squames in an operating room is not very large ($<< 10^{-3}$), collisions amongst the squames are neglected. The squame particle motion equation is that of Maxey & Riley (1983),

$$\frac{d}{dt}(\mathbf{x}_p) = \mathbf{u}_p \tag{12}$$

$$m_p \frac{d}{dt}(\mathbf{u}_p) = \mathbf{F}_g + \mathbf{F}_d + \mathbf{F}_\ell + \mathbf{F}_{am} + \mathbf{F}_p + \mathbf{F}_H, \tag{13}$$

where $\mathbf{x}_p$ is the particle (squames) centroid location, m_p is the mass of an individual particle, $\mathbf{u}_p$ is the particle velocity, $\mathbf{F}_g$ is the gravitational force, $\mathbf{F}_d$ is the drag force, $\mathbf{F}_\ell$ is the lift force, $\mathbf{F}_{am}$ is the added mass force, $\mathbf{F}_p$ is the pressure force, and $\mathbf{F}_H$ is the Basset history force.

The large ratio of particle density to air density, ρ_p/ρ_g, renders both the Basset history force and the added mass force negligible compared to the drag force. The ratio of the Saffman lift to the drag force is given by, $F_\ell/F_{drag} \sim \rho_g d_p^2 (du/dy)^{1/2}/\mu$, and is dependent on the shear rate and particle diameter. For particles with small diameter and low inertia this force can also be neglected in comparison to the drag force (Crowe *et al.*, 1996; Saffman, 1965). However, the lift force is incorporated in our calculations to account for the saltation of the squame particles from the operating room floor. The gravity, drag and lift forces are given as,

$$\mathbf{F}_g = (\rho_p - \overline{\rho}_g)\forall_p \mathbf{g}; \quad \mathbf{g} = -9.81 m/s^2 \tag{14}$$

$$\mathbf{F}_d = -\frac{1}{8}C_d\overline{\rho}_g\pi d_p^2|\mathbf{u}_p - \tilde{\mathbf{u}}_{g,p}|(\mathbf{u}_p - \mathbf{u}_{g,b}); \quad C_d = \frac{24}{Re_p}(1+0.15Re_p^{0.687}), \tag{15}$$

$$\mathbf{F}_\ell = -C_\ell m_p\frac{\overline{\rho}_g}{\rho_p}(\mathbf{u}_p - \tilde{\mathbf{u}}_{g,p}) \times (\nabla \times \tilde{\mathbf{u}}_g)_p; \quad C_\ell = \frac{1.61\times 6}{\pi d_p}\sqrt{\frac{\mu}{\overline{\rho}_g}|(\nabla \times \tilde{\mathbf{u}}_g)_p|} \tag{16}$$

where the subscript p represents the squame particle, $\tilde{\mathbf{u}}_{g,p}$ represents the fluid velocity interpolated at the particle center location, $\mathcal{V}_p$ is the particle volume, d_p is the particle diameter, $Re_p = \overline{\rho}_g|\mathbf{u}_p - \tilde{\mathbf{u}}_{g,p}|d_p/\mu$ is the particle Reynolds number, C_d is the drag coefficient, C_ℓ is the lift coefficient.

The gas-phase velocity, $\tilde{\mathbf{u}}_g$, in the particle equations above, is computed at individual particle locations within a control volume using a generalized, tri-linear interpolation scheme for arbitrary shaped elements. Introducing higher order accurate interpolation is straight forward; however, it was found that tri-linear interpolation is sufficient to represent the gas-phase velocity field at particle locations. As mentioned earlier, in LES of particle-laden flows, the particles are presumed to be *subgrid*, and the particle-size is smaller than the filter-width used. The gas-phase velocity field required in equations (12) and (13) is the total (unfiltered) velocity, however, only the filtered velocity field is computed in equations (4). The direct effect of the unresolved (subgrid) velocity fluctuations on particle trajectories depends on the particle relaxation time-scale, and the subgrid kinetic energy. Pozorski & Apte (2009) performed a systematic study of the direct effect of subgrid scale velocity on particle motion for forced isotropic turbulence. It was shown that, in poorly resolved regions, where the subgrid kinetic energy is more than 30%, the effect on particle motion is more pronounced. A stochastic model reconstructing the subgrid-scale velocity in a statistical sense was developed (Pozorski & Apte, 2009). However, in well resolved regions, where the amount of energy in the subgrid scales is small, this direct effect was negligible. In the present work, the direct effect of subgrid scale velocity on the droplet motion is neglected. However, it should be noted that the particles *do feel* the subgrid scale stresses through the subgrid model that affects the resolved velocity field. For well-resolved LES of swirling, separated flows with the subgrid scale energy content much smaller than the resolved scales, the direct effect is shown to be small (Apte *et al.*, 2003*b*, 2009). This is the main advantage of LES as compared to RANS. In RANS, only the time-average mean velocity is available, and all scales of turbulence affecting the instantaneous fluctuations around the mean

must be modeled. Approximating the effect of turbulent fluctuations on the particle dispersion is thus necessary for RANS, whereas, it is implicitly accounted for in the LES.

Equations (12,13) are integrated using a fourth-order Runge-Kutta time-stepping algorithm. After obtaining the new particle positions, the particles are relocated, particles that cross interprocessor boundaries are duly transferred, boundary conditions on particles crossing boundaries are applied, source terms in the gas-phase equation are computed, and the computation is further advanced. Solving these Lagrangian equations thus requires addressing the following key issues: (i) efficient search and location of particles on an unstructured grid (ii) interpolation of gas-phase properties to the particle location for arbitrarily shaped control volumes (iii) inter-processor particle transfer. The details on efficiently locating the particles on unstructured grids, search algorithms for particles, and interpolation schemes can be found in the work by Apte *et al.* (2003*b*, 2009).

In addition, if the squames impact internal boundaries, a simple, perfectly elastic specular reflection is assumed wherein the squames reverse the wall-normal velocity and preserve the wall-tangential velocity. If the squames impact the patient's knee or the inlet (suction port) of the 3M™ Bair Hugger™ blower system, they are assumed to stick to the surface and are no longer advanced in the computations.

3.3 Computational grid

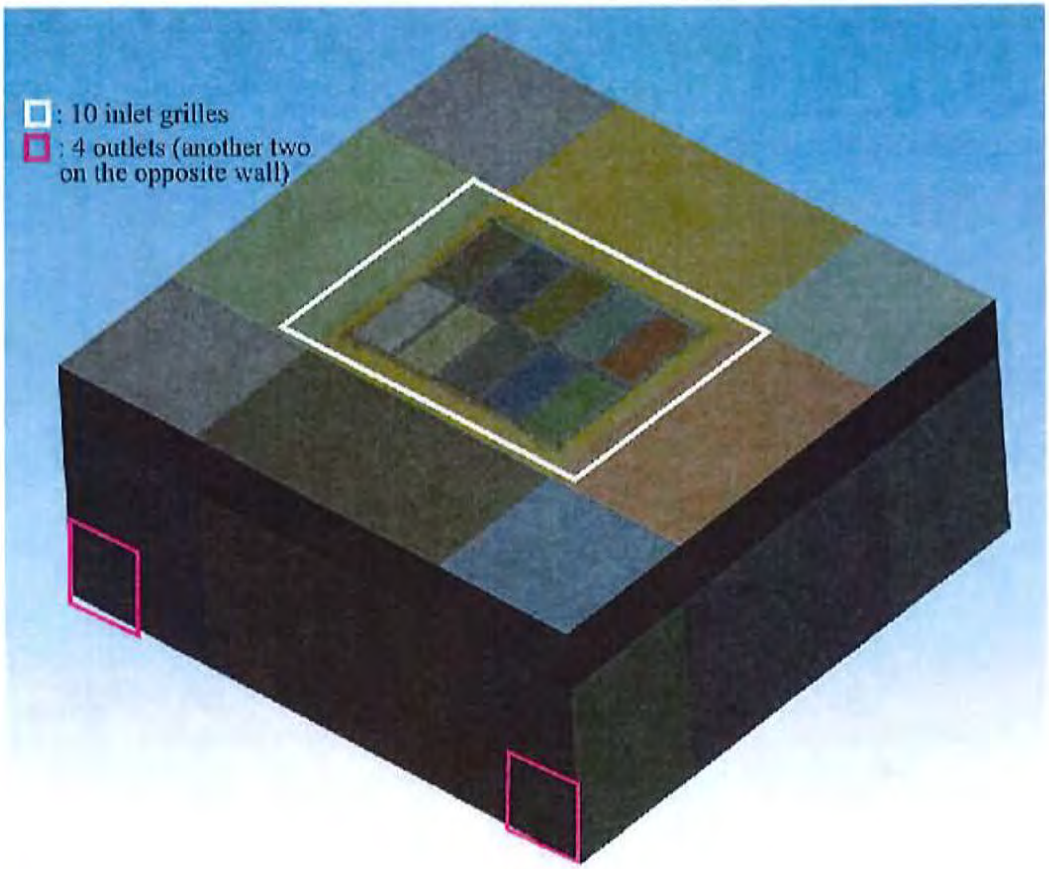
Use of high quality computational mesh is critical in LES for accurate prediction of the turbulent flow, but also having a stable numerical solution. However, to handle complex configurations, use of hybrid elements involving tetrahedrons, pyramids, hexagons and wedges, etc. is common in a typical computational grid. This helps with the grid generation surrounding complex features such as the operating table, the surgeons, the patient and the drape, for example. The transitions from one type of grid element to another; however, can lead to skewed elements. It is thus critical that the numerical algorithm be robust, stable and accurate at high Reynolds numbers on skewed or bad grid elements. A numerical algorithm developed for arbitrary shaped unstructured grids (Mahesh *et al.*, 2004; Ham *et al.*, 2003; Ham & Iaccarino, 2004; Mahesh *et al.*, 2006) that is based on kinetic energy conservation principles offers the much needed robustness and accuracy on such grids without resorting to explicit artificial dissipation. As discussed below, we use a research solver based on

such an algorithm.

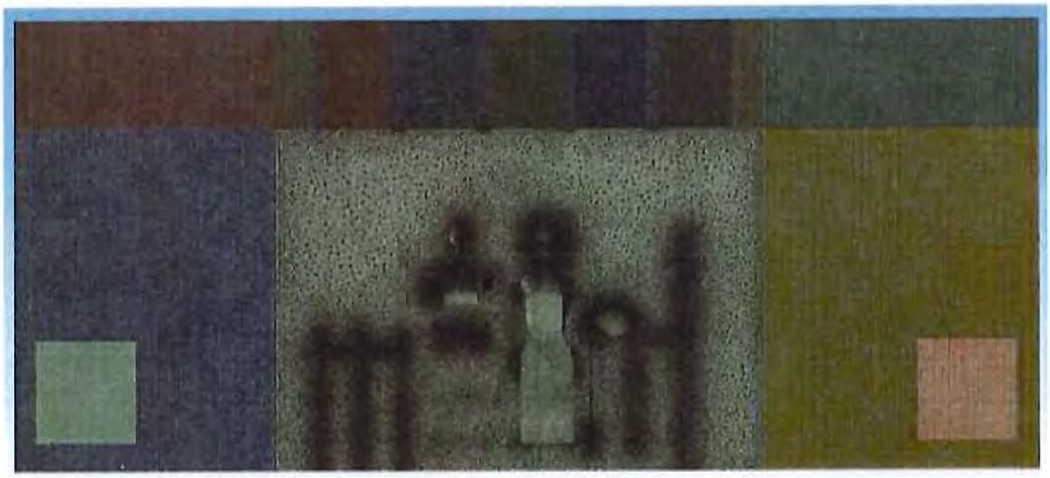
For the present study, a computational mesh (figure 8) was generated using the CAD model described earlier to facilitate predictive large eddy simulations. The mesh was generated using both tetrahedral and hexahedral cells. The transition of mesh from tetrahedral cells to hexahedral cells was done using a combination of pyramid and wedge type cells. Care was taken to generate a computational grid that minimizes the grid skewness as much as possible. As shown below, in the regions away from the complex OR configuration involving the surgeons, the tables, the patient and the drape, a mostly hex-dominant mesh is used. As one approaches closer to the operating table, the computational grid is transitioned to a predominantly tetrahedra-based mesh (see figure 8b). The total mesh count for the computational domain is about 66 million.

Figure 9 shows the grid resolution near the air inlet cross-sections. The grid is appropriately refined to capture the shear layer generated by the inlet flow between the grilles. The mesh surrounding the OR table, patient, surgeons, side tables, the blower, and surgical lamps is predominantly tetrahedral. The tetrahedral mesh was carefully refined to capture surface curvature. Extra refinement was performed near surfaces which were in close proximity to other surfaces. This enhanced mesh refinement is to ensures that the effect of surface shapes on the flow and particles going around them will be captured by the simulation (figure 10a,b.)

As is shown in the above figures, a high quality mesh was generated for the present LES investigation. The minimum tetrahedral cell size (defined as cube root of the cell volume) used near all key regions such as drape, patient, operating bed, surgeons, etc. was around 1mm. Smallest grid spacing in proximity regions resolving the gaps between closely placed surfaces is 0.7mm. The coarsest tetrahedral cell size used away from the key regions is 2.5cm. As mentioned earlier in the report a fine mesh was used near the inlet regions to resolve the flow entering the operating room. A uniform hexahedral cell size of 2.5cm was used to resolve the air inlet grille faces with 20 cells along its width and 44 cells along its length. The gaps between the inlet grilles were resolved using a finer mesh with each cell size of 0.63cm. To capture the inlet air flow structures properly, a refined uniform mesh of 0.38cm was used along the flow direction. Finally, a uniform cell size of 2.5cm was used to resolve each outlet grille with 28 cells along its width and 28 cells along its length. Various mesh metrics were checked to ensure that the quality of the generated mesh was good. Figure 11a shows histogram plot of cell skewness in the mesh. The average skewness was



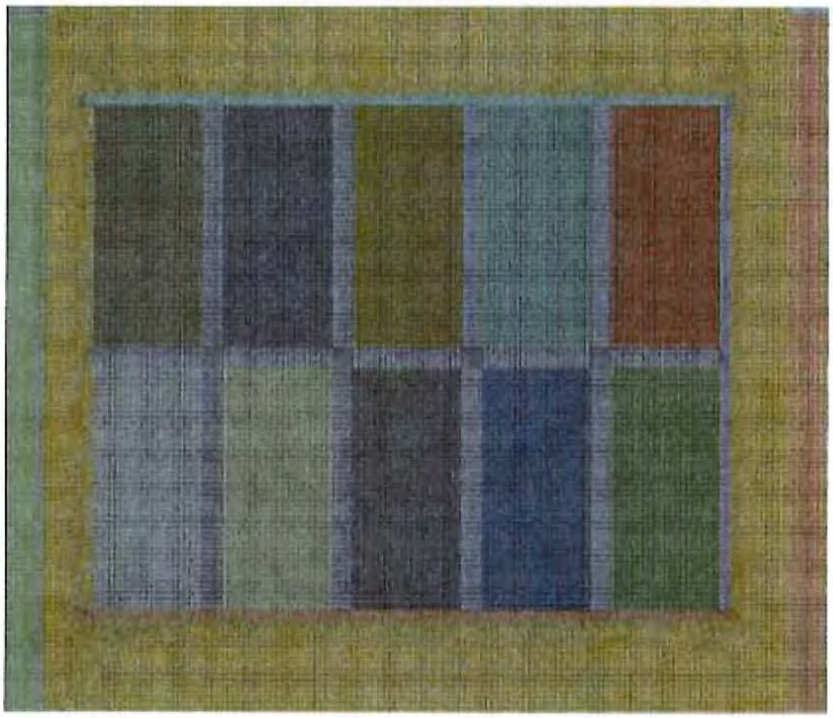
(a)



(b)

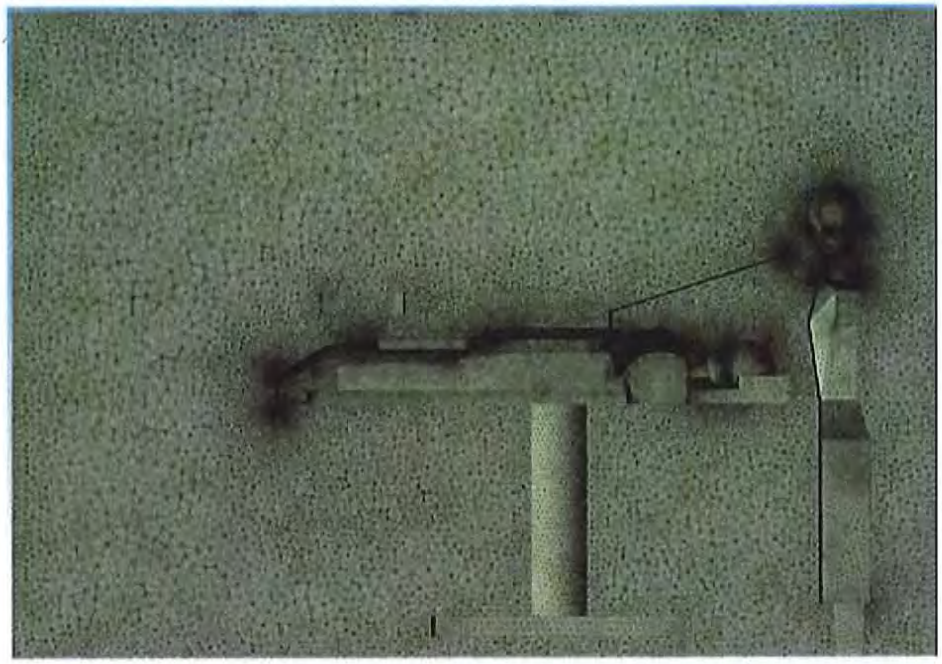
Figure 8: Computational mesh for the operating room model consisting of about 66M hybrid grid elements consisting of hexagons, tetrahedrons, pyramids and wedges: (a) the full 3D mesh, (b) cross-sectional slice showing hex-dominant mesh in the inlet and outlet regions and a tetahedral mesh near the operating table.

(a)

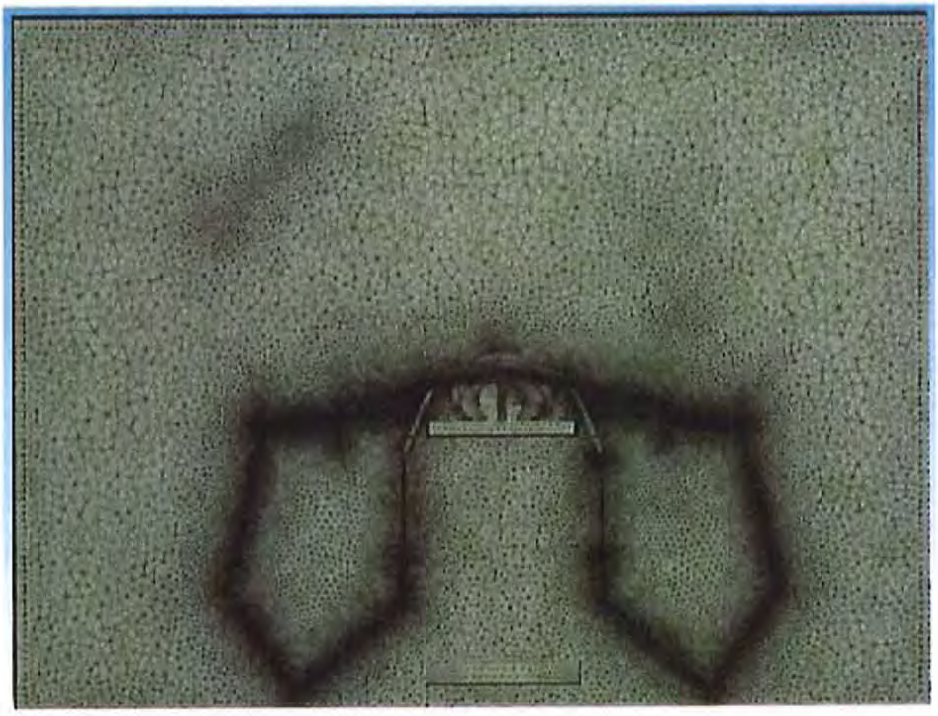


(b)

Figure 9: A cross section cut showing fine mesh near the ceiling of the room: (a) top view zoom-in, (b) top view showing all air inlet grilles.



(a)



(b)

Figure 10: Mesh refinement near curved surfaces and surfaces that are in close proximity to others: (a) side view showing the entire operating table, (b) side view showing drapes.

0.14 and with maximum skewness was 0.91. Only 0.018% of cells had total skewness greater than 0.8 indicating the high quality of cells in the mesh. Another mesh metric that was checked was the aspect ratio of cells. The maximum aspect ratio was 16.2 and the average cell aspect ratio was 2.9, which indicate that a majority of cells in the mesh were mostly uniform (see figure 11b).

3.4 Boundary Conditions

This subsection provides details of all boundary conditions used in the calculation, starting with operating room (OR) air inlet conditions, heat sources, BH hot air blower inflow (suction) and outflow, and OR air outlet conditions.

3.4.1 Inlet boundary conditions

The dimensions of the operating room are shown in Table 1. As shown, there are 10 inlet grilles supplying air. The net supply air volumetric flow rate, $\dot{V}$, is 1.10436 m^3/s (0.39 ft^3/s). Using the inlet flow rates, the air changes per hour (ACH) of the room is calculated as follows,

$$\text{ACH} = \dot{V} \times 3600/(LWH) = 24.45 \text{ per hour}, \tag{17}$$

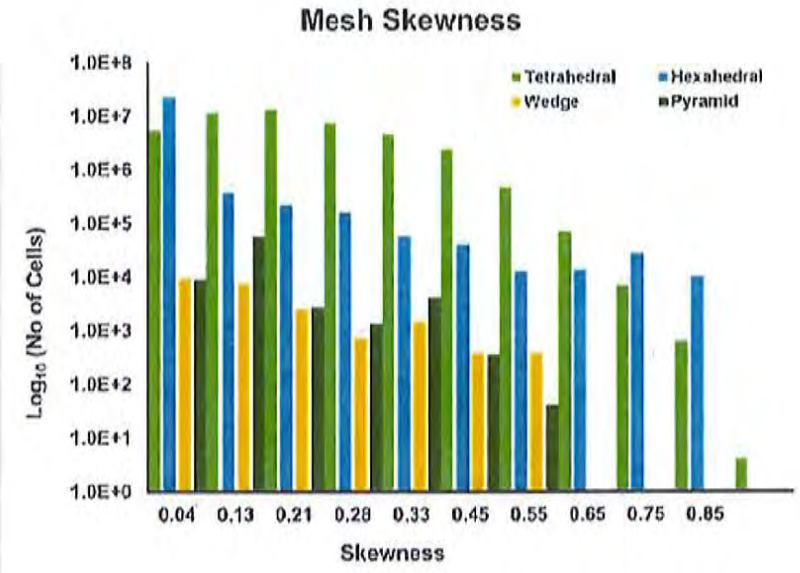
where L, W and H are the room length (in x), width (in y) and height (in z) directions. The ACH is according to the ASHRAE handbook Memarzadeh & Manning (2002), which suggests the ACH to be about 25 per hour for an operating room with recirculating air system.

The inlet boundary conditions are imposed at the 10 grilles on the ceiling of the operating room to model the inlet part of the forced ventilation system. The average inlet velocity, $\overline{U}_{in}$, is found to be 0.1933m/s based on,

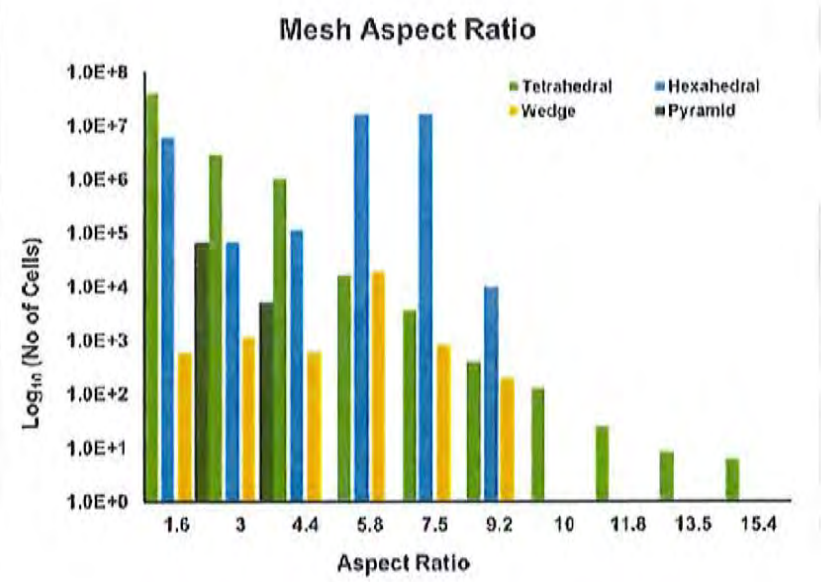
$$\overline{U}_{in} = \dot{V}/(10 \times A_{grill}), \tag{18}$$

where A_{grill} is the area of the cross-section ($1.12 \times 0.51 = 0.5712 m^2$) and $\dot{V} = 1.1044 m^3/s$ ($39 ft^3/s$) is the net inlet volumetric flow rate. The air temperature of the inlet flow, T_{in}, is set to 59°F (15°C).

Based on Reynolds number for the inlet grilles, $Re_{in} = 9226.54$ (Table 1), the inlet flow is turbulent. In order to have completely predictive numerical simulation and to minimize the effect of boundary conditions, it is necessary to impose a proper, fully developed turbulent flow field at the in-



(a)



(b)

Figure 11: Statistics histograms of the quality of mesh used in the computation: (a) skewness, (b) aspect ratio.

Table 1: Operating room characteristics

Parameter	Value
Room dimensions [m], L, W, H	$7.315 \times 7.00 \times 3.175$
Supply air flow rate [m^3/s], $\dot{V}$	1.10436
ACH [$1/hr$]	24.45
Room air temperature [°C]	15
Inler air density [kg/m^3], ρ_{in}	1.225
Supply air temperature [°C]	15
Room air pressure [Pa]	1.0131×10^5
Grille dimensions [m]	1.12×0.51
Grille Area [m^2]	0.5712
Grille hydraulic diameter [m], D_h	0.7
Mean inlet velocity [m/s], $\overline{U}_{in}$	0.1933
Inlet Reynolds number, $Re_{in} = \frac{\rho_{in}\overline{U}_{in}D_h}{\mu}$	9226.54

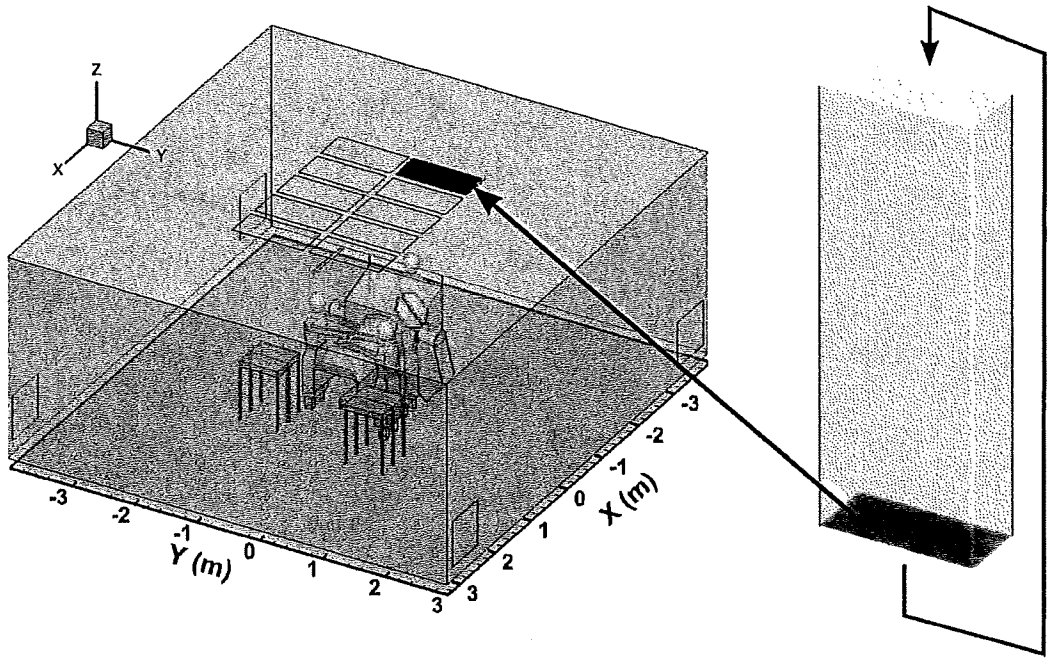


Figure 12: Schematic of the periodic duct used to generate inlet flow data.

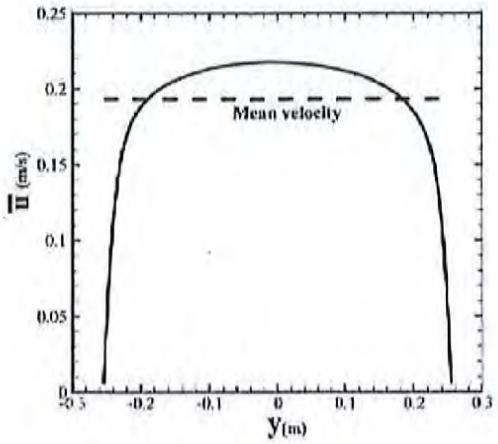


Figure 13: Mean velocity profile generated by a periodic duct flow for the inlet grilles.

let. Thus, a periodic turbulent duct flow was computed (figure 12) to produce a target mean flow rate equal to that prescribed ($\dot{V} = 1.10436\text{m}^3/\text{s}$) using a body force technique of Pierce & Moin (1998*b*). This also generates turbulence fluctuations at the inlet plane that satisfy the continuity equation. The cross-sectional area of the periodic duct used is the same as that of each grille ($1.12\text{m} \times 0.51\text{m}$), and the length is about 4.5 times the hydraulic diameter of the cross-section. The velocity field data at the inlet cross-section was recorded in time series for almost 400 seconds of physical time. Figure 13 shows the time-averaged velocity field in the center plane of the duct obtained from the periodic duct simulation. The turbulence intensity ($I = \sqrt{\frac{1}{3}(u_{rms}^2 + v_{rms}^2 + w_{rms}^2)}/\overline{U}_{in}$) at the inlet cross-section is 5-6% of the mean inlet velocity ($\overline{U}_{in}$), and is in agreement with the experimental measurements conducted by McNeill *et al.* (2012, 2013). Here, u_{rms}, v_{rms} and w_{rms} are the root-mean square velocity components in the x, y and z directions, respectively.

3.4.2 Hot air blower and other heat sources

A 3M™ Bair Hugger™ 750 blower draws air from the floor of the operating room, heats it and blows it into the blanket (3M™ Bair Hugger™ Model 522) that covers the torso region of the patient. The blanket is covered with a plastic drape. The maximum flow rate of the blower is $\dot{V}_{\text{blower}} = 0.021\text{m}^3/\text{s}$. The hot air moves along the surface of the drape that faces the patient and then it is discharged into the room along the drape edges. In the present calculation, the bottom surface (facing the floor) of the 3M™ Bair Hugger™ blower is considered as a suction surface with

surface area ($A_{extraction} = 0.03796\text{m}^2$). A Dirichlet boundary condition is applied at this surface that prescribes the extraction velocity $\overline{U}_{extraction}$ as

$$\overline{U}_{extraction} = \frac{\dot{V}_{blower}}{A_{extraction}}, \tag{19}$$

giving an extraction velocity of 0.5532m/s. To model the hot air discharged along the edges of the drape. The total area of this edge of the drape is measured to be $A_{drape} = 0.07794\text{m}^2$. A Dirichlet boundary condition is applied such that the air is injected into the room perpendicular to the edges of the drape with velocity, $\overline{U}_{drape}$, calculated as,

$$\overline{U}_{drape} = \frac{\dot{V}_{blower}}{A_{drape}}, \tag{20}$$

giving an average injection velocity along the drape edge as 0.2694 m/s. The temperature of the hot air at the BH blower outlet is prescribed equal to 109°F (42.77°C) and the temperature of the air leaving the drape edge is set equal to 106°F (41.11°C) according to 3M video at: https://www.youtube.com/watch?v=QhzeInWIJ54. The flow rates at the inlet grilles and for the blower are summarized in Table 3.4.2.

Other heat sources in the surgical room are mainly the surgeons, patient, surgical lamps, and exposed surface of the patient's knee. These heat sources can cause warming of the air in contact with the surfaces and result in a rising thermal plume. For these surfaces, a Dirichlet condition was used for temperature based on the experimentally measured values. In their work, McNeill *et al.* (2012) conducted detailed measurements of detailed surface temperatures that may lead to buoyant plumes specifically to be used in CFD calculations. The values are summarized in Table 3.4.2, among which, the temperatures of surgeons and patient's heads as well as the surgical lamps are based on the work of McNeill *et al.* (2012) and the rest are from the *3M video*. For all other other solid surfaces, a no heat flux Neumann condition was specified, $\frac{\partial T}{\partial n} = 0$.

3.5 Numerical solution method

The computational approach is based on a co-located, finite-volume, energy-conserving numerical scheme on unstructured grids (Moin & Apte, 2006; Mahesh *et al*, 2006) and solves the variable

Table 2: Flow and temperature conditions

Parameter	Value
Inlet volume flow rate $\dot{V}$, [m^3/s]	1.1044
Temperature of inlet grille air, [°C]	15
Mean inlet velocity [m/s], $\overline{U}_{in}$	0.1933
BH blower volume flow rate $\dot{V}_{blower}$, [m^3/s]	0.021
Temperature of hot air leaving the drape edge, [°C]	41.11
Heads of the surgeons and patient, [°C]	31.44
The patient's knee , [°C]	37.78
Two surgical lamps, [°C]	93.92

density gas-phase flow equations in the limit of zero-Mach number. In this co-located scheme, the velocity and pressure fields are stored and solved at the centroids of the control volumes. Numerical solution of the governing equations of the continuum fluid phase and particle phase (squames) are staggered in time to maintain time-centered, second-order advection of the fluid equations. Denoting the time level by a superscript index, the velocities are located at time level t^n and t^{n+1}, and pressure, density, viscosity, and the scalar fields at time levels $t^{n+3/2}$ and $t^{n+1/2}$. Sqaumes position and velocity are advanced explicitly from $t^{n+1/2}$ to $t^{n+3/2}$ using fluid quantities at time-centered position of t^{n+1}.

3.5.1 Advancing the Lagrangian squames equations

The squames (particles) equations are advanced using a fourth-order Runge-Kutta scheme. Owing to the disparities in the flow field time-scale (τ_f) and the squames relaxation time (τ_p) sub-cycling of the squames equations may become necessary. Accordingly, the time-step for squames equation advancement (Δt_p) is chosen as the minimum of τ_p and the time-step for the flow solver (Δt). For the present simulations, the squames relaxation time, τ_p, based on the drag force, was found to be always larger than the time-step, Δt, used for solving the fluid flow equations in LES. Thus, the temporal evolution of the squames was well resolved by the flow time step, and subcycling of the particle equations was not necessary.

After obtaining their new positions, the squames are relocated, and the squames that cross inter-processor boundaries are duly transferred. Boundary conditions for squames crossing boundaries are applied and the computation is further advanced. Solving these Lagrangian equations thus requires

addressing the following key issues: (i) efficient search for locations of squames on an unstructured grid, (ii) interpolation of gas-phase properties to the squames location for arbitrarily shaped control volumes, (iii) inter-processor transfer of the squames.

Locating the squames particles in a generalized-coordinate structured code is straightforward since the physical coordinates can be transformed into a uniform computational space. This is not the case for unstructured grids used in the present simulations (Apte *et al.*, 2003*b*,*a*, 2009). The approach used here, projects the squames location onto the faces of the control volume and compares these vectors with outward face-normals for all faces. If the particle lies within the cell, the projected vectors point the same way as the outward face-normals. This technique is found to be very accurate even for highly skewed elements. A search algorithm is then required to efficiently select the control volume to which the criterion should be applied. An efficient technique termed as 'the known vicinity algorithm' was used to identify the control volume number in which the particle lies. Given the previous particle location, the known-vicinity algorithm identifies neighboring grid cells by traversing the direction the particle has moved. In LES, the time steps used are typically small in order to resolve the temporal scales of the fluid motion. Knowing the initial and final location of the particle, this algorithm searches in the direction of the particle motion until it is relocated. The neighbor-to-neighbor search is extremely efficient if the particle is located within 5-10 attempts, which is usually the case for 98% of the squames in the present simulation. Once this cell is identified, the fluid parameters are interpolated to the particle location using a generalized, tri-linear interpolation scheme for arbitrary shaped elements. Introducing higher order accurate interpolation is straight forward; however, it was found that tri-linear interpolation is sufficient to represent the gas-phase velocity field at particle locations. In the present case, particles are distributed over several processors used in the computation, and the load-imbalance was not significant. Details of the algorithm can be found in Apte *et al.* (2003*b*, 2009). The overall increase in computational cost due to addition of about 3 million particles was about 25% per time-step.

3.5.2 Advancing the Eulerian fluid flow equations

The scalar field (enthalpy or non-dimensional temperature; equation 5) is advanced using the old time-level velocity field. A second-order WENO scheme is used for scalar advective terms and centered differencing for the diffusive terms. All terms, except the source terms due to buoyancy

effect, are treated implicitly using Crank-Nicholson for temporal discretization. Once the scalar field is computed, the density and temperature fields are obtained from constitutive relations (equation 7) and the ideal gas law (equation 2). The cell-centered velocities are advanced in a predictor step such that the kinetic energy is conserved. The predicted velocities are interpolated to the faces and then projected. Projection yields the pressure at the cell-centers, and its gradient is used to correct the cell and face-normal velocities. The steps involved in solving the projection-correction approach for velocity field are briefly described below, Details of this algorithm may be found in Moin & Apte (2006); Mahesh *et al.* (2006); Apte *et al.* (2008*b*).

- Advance the fluid momentum equations using the fractional step algorithm. The density field is available at intermediate time level is obtained from arithmetic average at the two time steps $t^{n+3/2}$ and $t^{n+1/2}$.

$$\frac{\rho u_i^* - \rho u_i^n}{\Delta t} + \frac{1}{2V_{cv}} \sum_{\text{faces of cv}} \left[u_{i,f}^n + u_{i,f}^* \right] g_N^{n+1/2} A_f = \tag{21}$$

$$\frac{1}{2V_{cv}} \sum_{\text{faces of cv}} \mu_f \left(\frac{\partial u_{i,f}^*}{\partial x_j} + \frac{\partial u_{i,f}^n}{\partial x_j} \right) A_f + (\rho - \rho_0) g_i$$

where f represents the face values, N the face-normal component, $g_N = \rho u_N$, and A_f is the face area. The superscript '$*$' represents the predicted velocity field, and $g_N^{n+1/2} = 0.5(g_N^n + g_N^{n+1})$.

- Interpolate the velocity fields to the faces of the control volumes and solve the Poisson equation for pressure:

$$\nabla^2 (p\Delta t) = \frac{1}{V_{cv}} \sum_{\text{faces of cv}} \rho_f u_{i,f}^* A_f + \frac{\rho^{n+3/2} - \rho^{n+1/2}}{\Delta t} \tag{22}$$

- Reconstruct the pressure gradient, compute new face-based velocities, and update the cv-velocities using the least-squares interpolation used by Mahesh *et al.* (2004); Ham *et al.* (2003); Mahesh *et al.* (2006),

$$\frac{\rho \left(u_i^{n+1} - u_i^* \right)}{\Delta t} = -\frac{\delta p}{\delta x_i}. \tag{23}$$

4 Results

The numerical simulation was initiated with stagnant air (zero velocity) in the operating room and proper boundary conditions. A simulation was carried out with the blower off and all surfaces at room temperature for about 67s of physical time, which corresponds to about 4 flow through times based on the average inlet air velocity and the height of the room. After the initial transients, the thermal boundary conditions were applied at the surgeons heads, the patient's knee, the surgical lights. A calculation was performed for another 54s to establish a stationary flow with the thermal plumes created by the surfaces with higher-than-ambient temperatures. At this time, calculation of statistics for time-averaged mean velocity field and turbulence intensity were initiated and also 3 million squame particles were placed at the floor in three different regions surrounding the operating table as described below. With the blower-off the time-step used in the calculation was $\Delta t = 6 \times 10^{-5}$s giving a CFL number of about 0.75. This time step was able to resolve the important time-scales of turbulence and particle motion accurately. The flow statistics were collected for a total of 80s after a stationary flow field was established and the squames trajectories were calculated for about 21s.

After the above calculation was completed, the remaining squames particles in the computational domain were removed, and the blower was turned on. With the blower discharging a hot air at higher speeds, the time-step was reduced by a factor of 2.5 to $\Delta t = 2.4 \times 10^{-5}$s maintaining the CFL number about 0.6. The reduction in time step is related to both the explicit treatment of the gravitational source term in the momentum equation as well as increased velocity at the blower discharge location. A calculation was performed for about 30s to obtain a developed plume from the hot air discharged by the blower. Flow statistics and the initial location of 3 million squames particles were initiated. With the blower-on, the flow statistics were collected for about 37s and particle trajectories were calculated for about 30s.

All calculations were performed on a parallel computer and used 1600 processors. The computational domain was decomposed such that each processor contains roughly the same number of control volumes. The overall calculation (including initial transient, the case with blower-off and the case with blower-on including particle trajectories for both cases) took about 2M CPU-hrs. For the case of blower-off, about 20s of physical time would cost roughly 100,000 CPU-hours, whereas

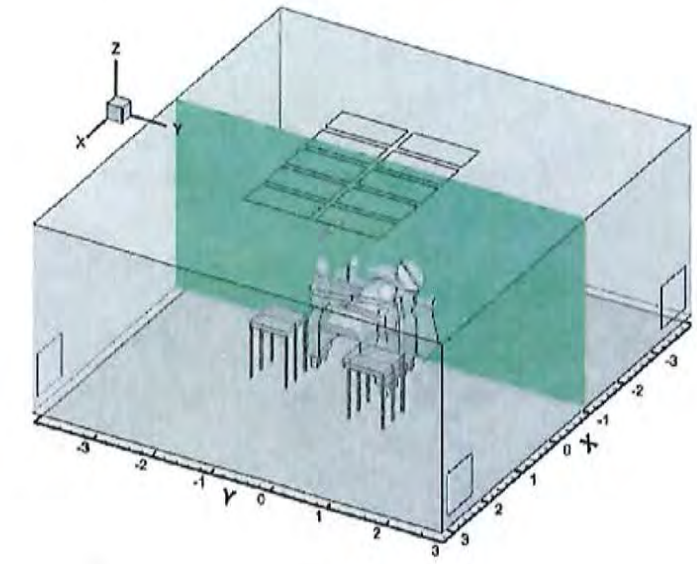
the same calculation with blower-on would cost roughly 220,000 CPU-hours. For each case, tracking 3 million trajectories of squames would add about 20-30% additional computing cost. This is because, initially the 3 million squames are clustered in a small region near the floor causing load imbalance as the particles were present on only a few processor domains. The flow statistics and particle trajectories are discussed below.

4.1 Flow characteristics

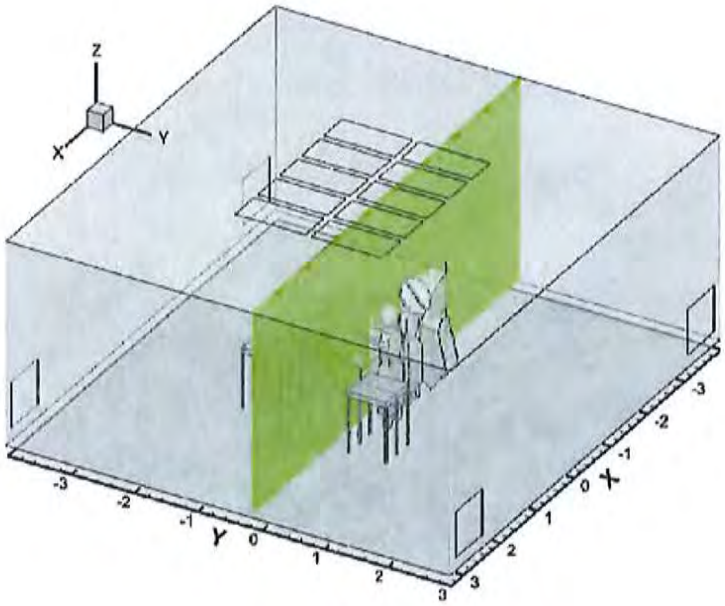
Figures 14a and 14b show the locations of two slices through the three-dimensional computational domain at $x = -0.88$m and $y = -0.162$m for which the mean velocity magnitude, turbulence intensity, and instantaneous temperature contours are plotted. The $x = -0.88$m slice shows a planar cut that includes the surgical lamp and the operating table (OT). The $y = -0.162$m slice shows a side view and contains 2 medical staff, a side table, the surgical lamp, and part of the inverted U-shaped drape. For these two slices, the flow characteristics with blower-off and blower-on are compared.

Figures 15, 16, and 17 show the contours of mean velocity magnitude, turbulence intensity, and instantaneous temperature, respectively, for the two cases of blower-off and blower-on. For the case of blower-off, figure 15a shows that the ventilation air from the ceiling inlet grilles moves downwards, gets deflected by the surgical lights and the table, impinges on the floor farther away from the table, and finally exits through the outlet grilles. Large recirculation regions are created on both sides of the table. The flow is not symmetric owing to asymmetries in the configuration itself. In comparison, with the blower turned on, the flow underneath and around the table is considerably modified as can be seen from the large velocity magnitudes under the table (figure 15b). The recirculation region is also disrupted by the rising air from the hot blower discharge. This difference is clearly visible from the turbulence intensity contours shown in figure 16a,b. With the blower-off, the maximum turbulence intensity level is about 30% in the high shear regions between the inlet air streams, as well as near the warm surgical lights due to the buoyant plume. With the blower-on, the turbulence intensity level is as high as 60% in regions affected by the rising thermal plumes from the blower hot air. The instantaneous temperature contours shown in figure 17a,b confirm that the increased turbulence level is mainly because of the thermal plumes from the hot blower air as can be seen by the high temperature regions under the OT.

Figures 18, 19, and 20 show the contours of mean velocity magnitude, turbulence intensity, and

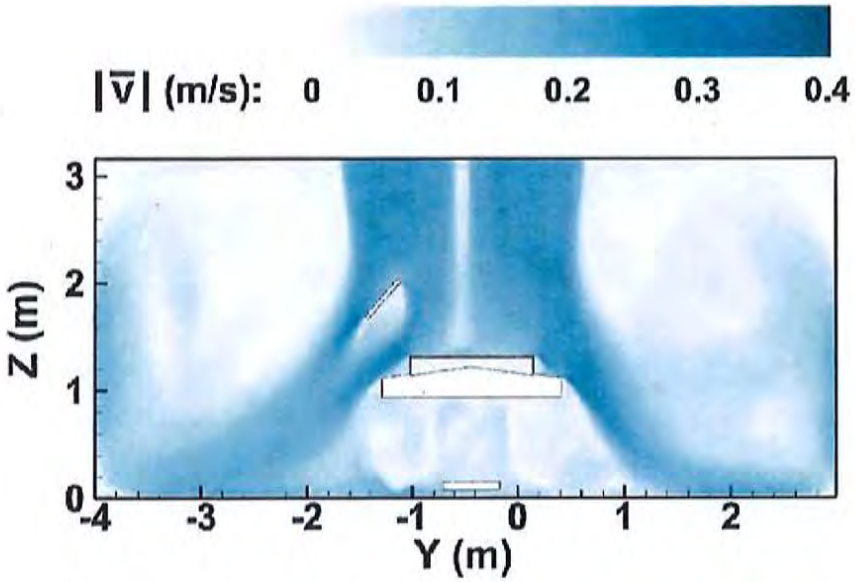


(a)

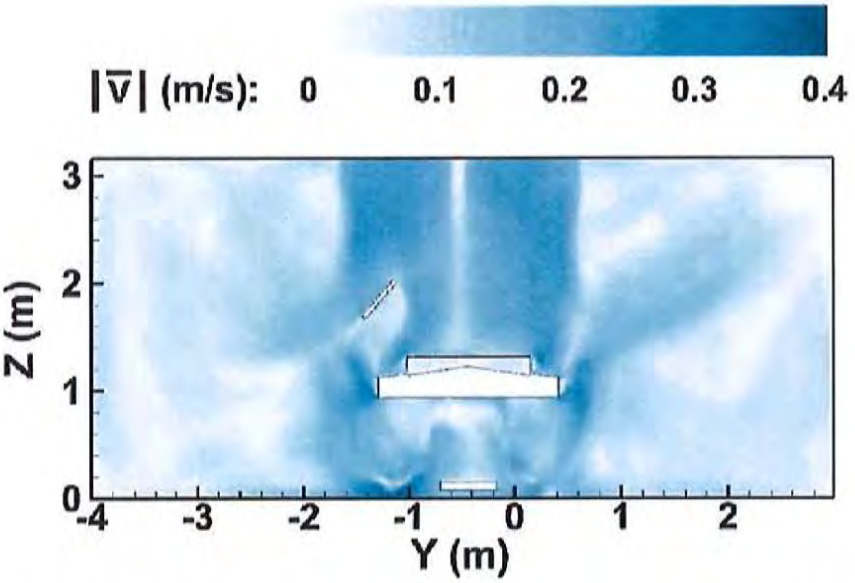


(b)

Figure 14: Locations of the planes for which contour plots of mean velocity magnitude, turbulence intensity and instantaneous temperature are presented to compare the effect of the blower discharge on the flowfield: (a) $x = -0.88$m (b) $y = -0.162$m.

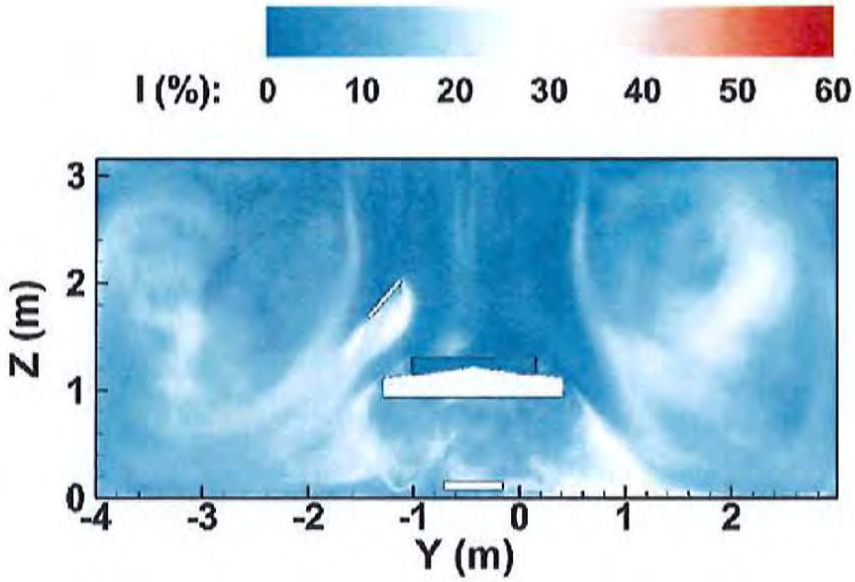


(a)

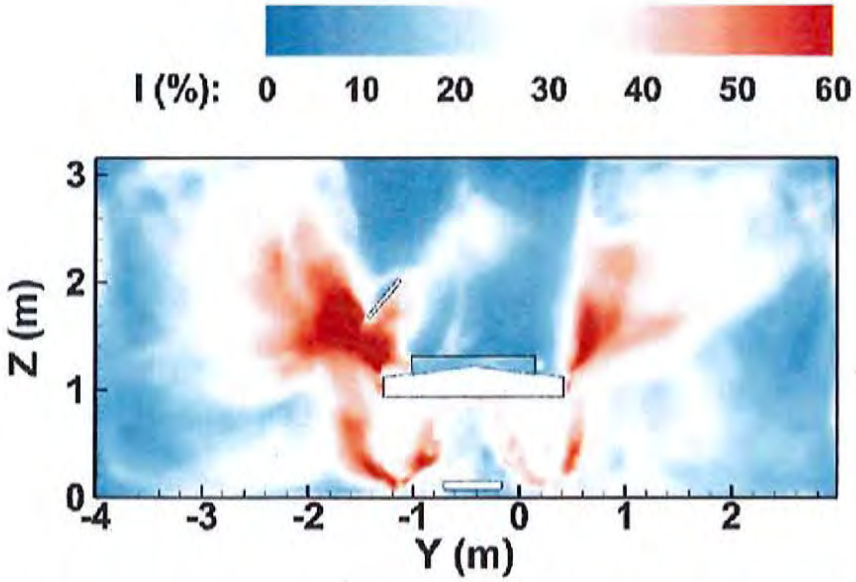


(b)

Figure 15: Contours of the mean velocity magnitude at $x = -0.88$m (a) with blower-off and (b) with blower-on. The time average is taken over a physical time of 80s (no blower) and 37s (with blower) after establishing a stationary state.

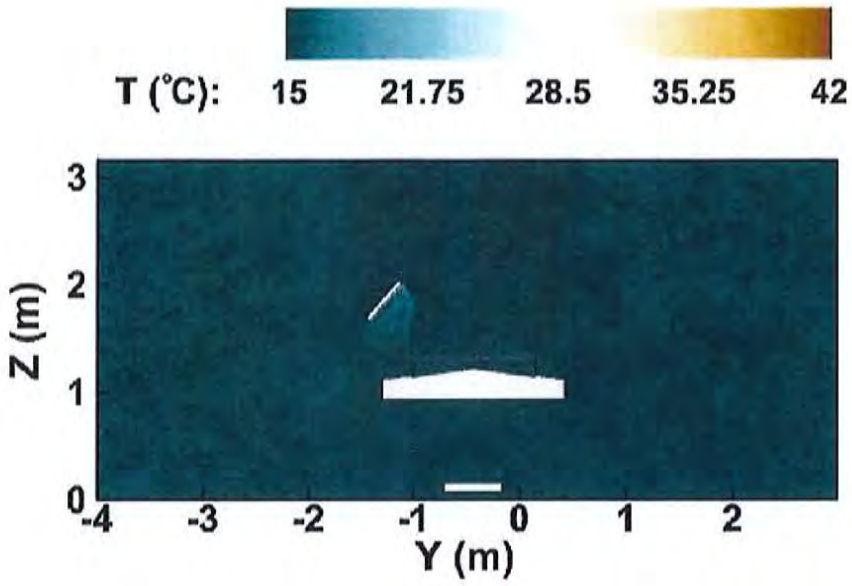


(a)

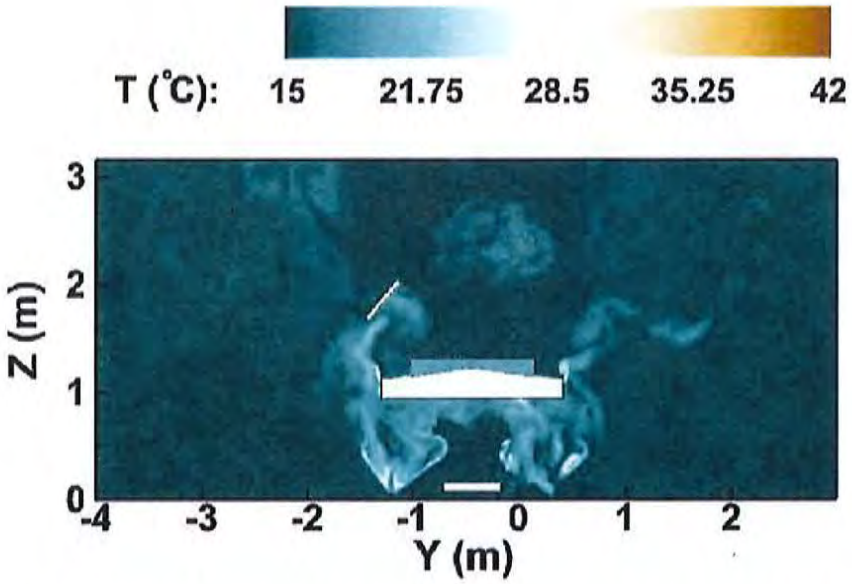


(b)

Figure 16: The turbulence intensity contours at $x = -0.88$m (a) with blower-off and (b) with blower-on. The time average is taken over a physical time of 80s (no blower) and 37s (with blower) after establishing a stationary state.



(a)



(b)

Figure 17: The instantaneous temperature contours at $x = -0.88$m (a) with blower-off and (b) with blower-on. These snapshots are at about 35s after a stationary flow field was obtained and calculation for flow statistics was initiated.

instantaneous temperature, respectively, for the cases of blower-off and blower-on at $y = -0.162$m. Similar trends as described before are observed. The hot blower air and the rising thermal plumes disrupt the downward ventilation air flow. The high temperatures and turbulence intensity under the inverted U-shaped drape are clearly visible. The flow is also highly asymmetric with the blower turned on owing to the orientation and location of the drape. It is also seen from figure 20b that the rising thermal plumes may reach the ceiling in some regions. With the blower off, however, the plumes from warm surfaces of surgical lights, surgeons heads, and patient's knee are weak and are not significant enough to disrupt the downward ventilation air flow.

4.2 Dispersion of squames

This section provides details of the initial locations of the squames, their trajectories, and statistics of sampling the particles in regions of interest with high potential of reaching the surgical site.

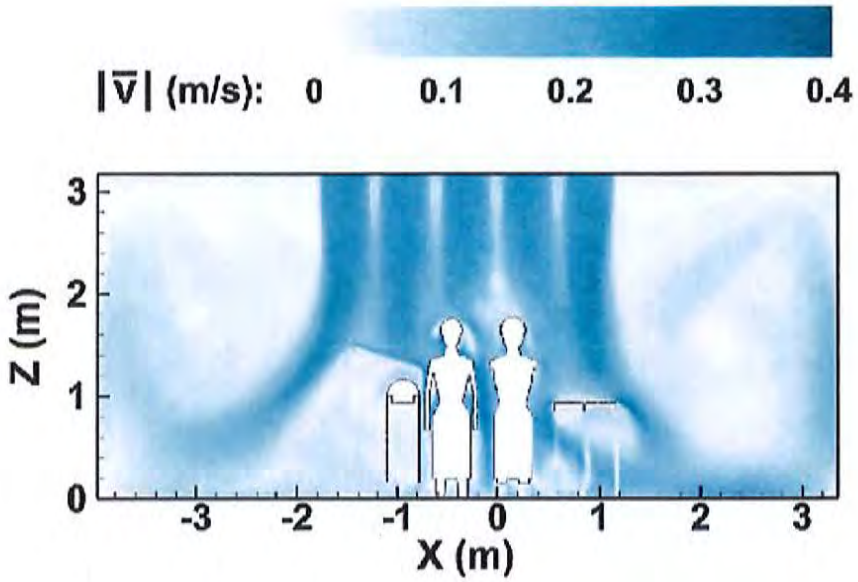
4.2.1 Initial locations of squames

In order to provide a worst-case (or least probable) scenario for the squames to be carried to the surgical site by the air convection, all 3 million squames were initially placed on the floor and randomly distributed in a small region surrounding the operating table within a height of about 1 cm above the floor of the OR. If these squames are lifted by the turbulent air and moved to the surgical site, other effects such as motion of medical equipment and staff, additional squames shed from the heads and faces of medical staff, surgical garments, etc. will have an even higher probability to reach the surgical site.

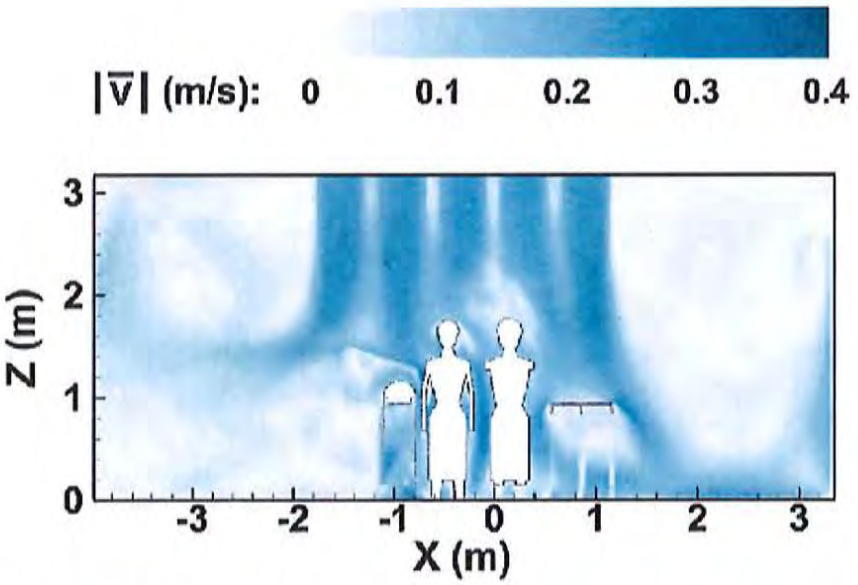
Table 3: Coordinates of color-coded regions for initial positions of squames as shown in figure 21.

Color-coded initial position	$(x, y, z)_{min}$ [m]	$(x, y, z)_{max}$ [m]
Red	(-1.40, -0.025, 0.0)	(0.70, 0.40, 0.01)
Green	(-1.80, -1.35, 0.0)	(-1.4, 0.4, 0.01)
Yellow	(-1.40, -1.35, 0.0)	(0.70, -0.855, 0.01)

Three million particles with a diameter of 10 micron are placed within a 1 cm thick layer above the floor of the OR. The region where the particles are located is around the OT, surrounding the feet of four surgeons present in the CAD model. To better visualize the trajectories the squames

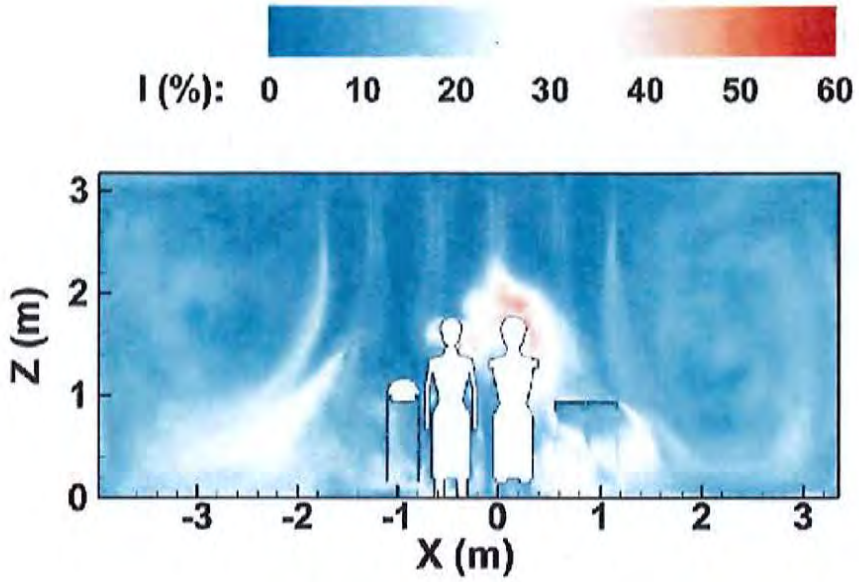


(a)

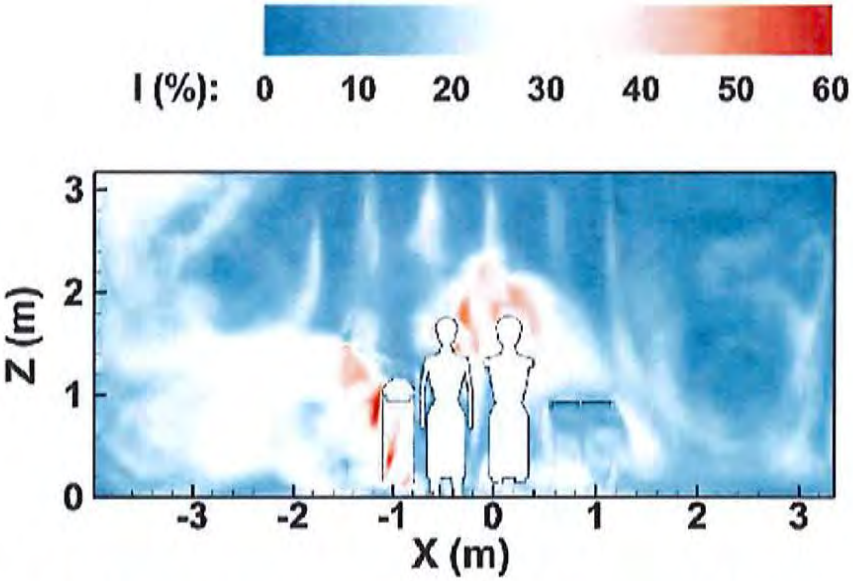


(b)

Figure 18: Contours of the mean velocity magnitude at $y = -0.162$m (a) with blower-off and (b) with blower-on. The time average is taken over a physical time of 80s (no blower) and 37s (with blower) after establishing a stationary state.

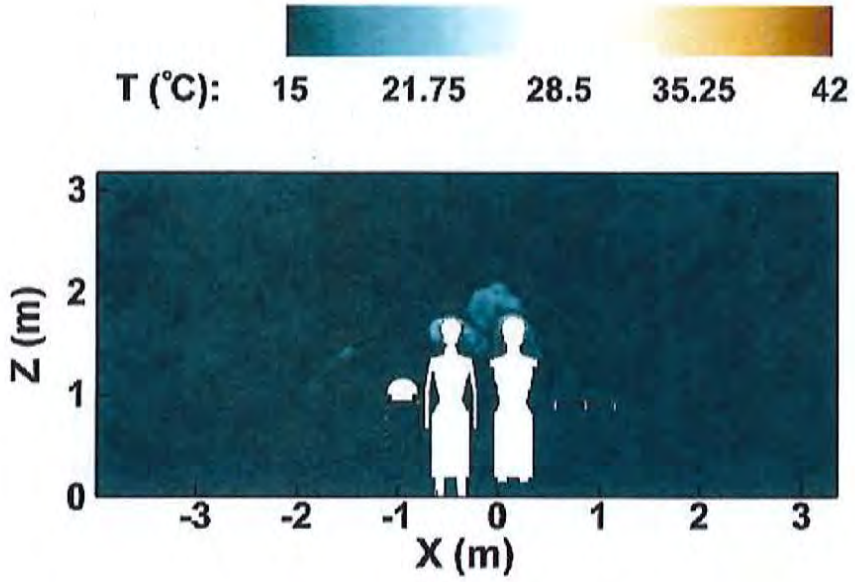


(a)

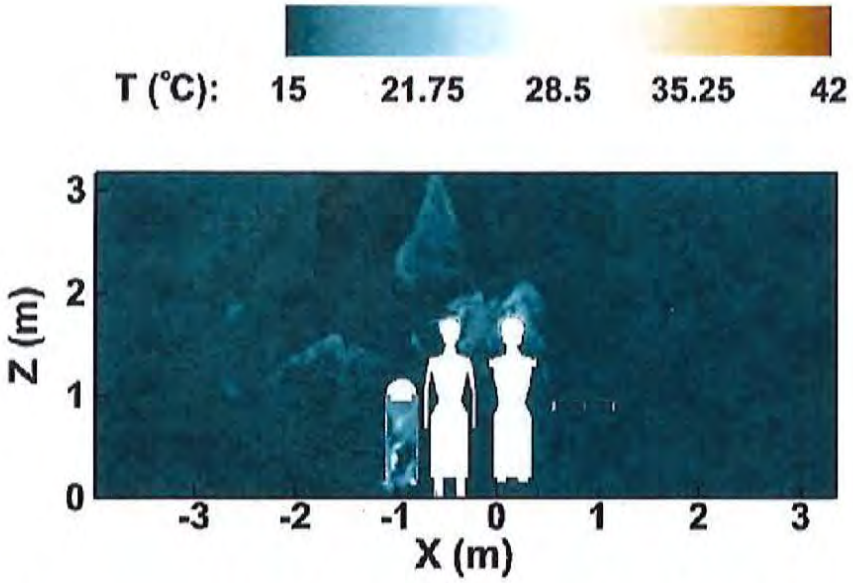


(b)

Figure 19: The turbulence intensity contours at $y = -0.162$m (a) with blower-off and (b) with blower-on. The time average is taken over a physical time of 80s (no blower) and 37s (with blower) after establishing a stationary state.



(a)



(b)

Figure 20: The instantaneous temperature contours at $y = -0.162$m (a) with blower-off and (b) with blower-on. These snapshots are at about 35s after a stationary flow field was obtained and calculation for flow statistics was initiated.

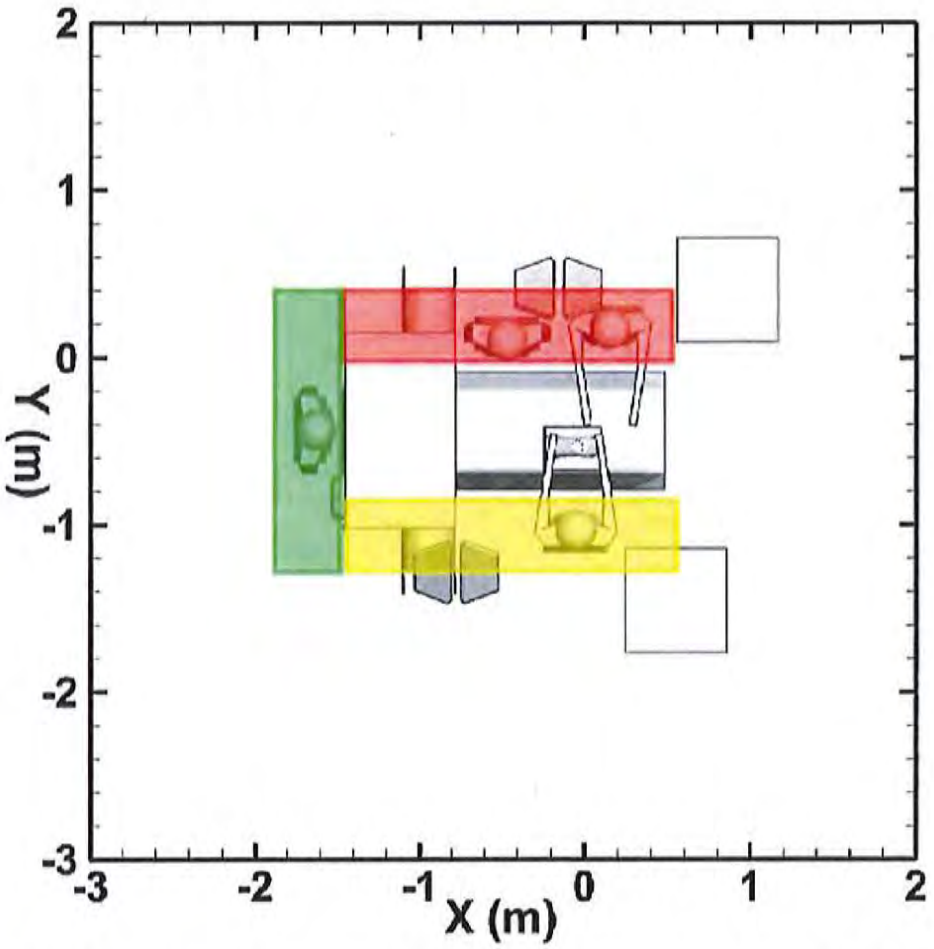


Figure 21: Three color-coded regions where the 3 million squames were initially distributed within a 1 cm height from the floor.

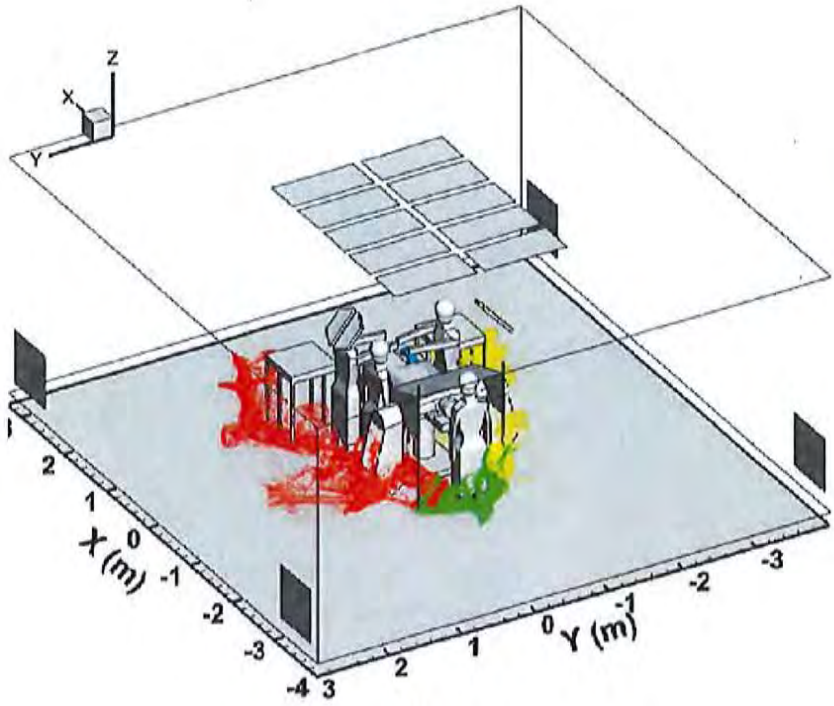
from different initial locations, the U-shaped region is divided into three rectangular sections color-coded as (i) red, (ii) green and (iii) yellow as shown in figure 21. One million squames are placed in each of the three sections at the same time, providing equal probability for the statistical analysis of motion of squames. The position of an individual squame particle in a section is chosen randomly using a uniform distribution. The squames of each section are tagged with distinct IDs. The actual coordinates of the three sections are given in Table 3.

4.2.2 Trajectories and snapshots of squames

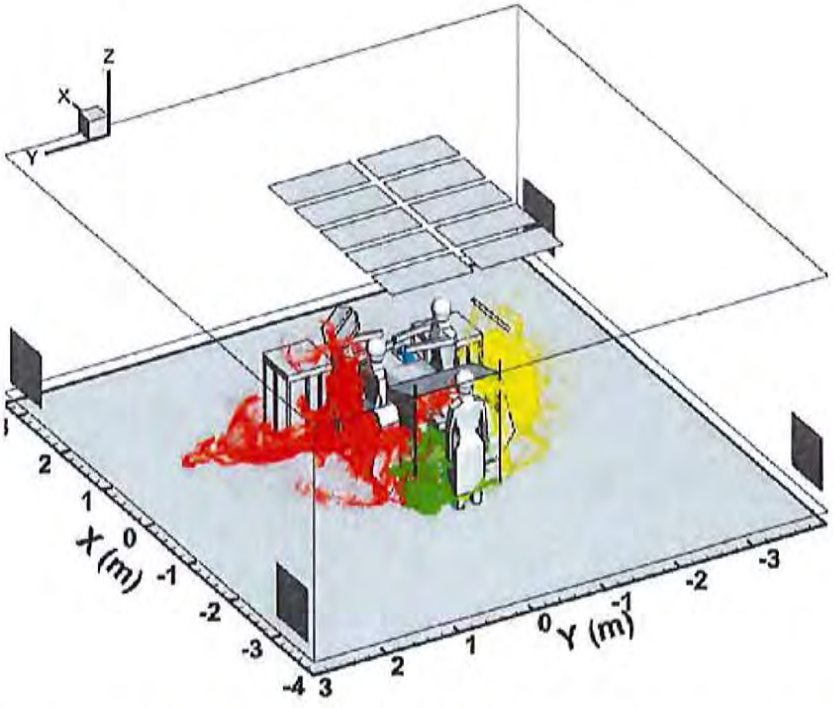
In order to visualize the effect of the hot blower air on the trajectory of squames, instantaneous scatter plots of squames are displayed at 10s and 20s after their initiation with blower-off and blower-on in figures 22a,b and 23a,b, respectively. The squames are also color-coded based on their region of origin as highlighted in figure 21. Drastic differences between the blower-off and blower-on cases are observed. It is clear from figures 23a that the majority of the squames are dispersed by the ventilation air flow towards the outlet grilles when the blower is off. None of the squames actually rise to the level of the side tables or the OT. In contrast, in the case of blower-on, a large number of squames are lifted upwards by the rising thermal plumes. Some of the squames (mostly red-colored and some yellow-colored) are lifted above the surgeons heads and are blown towards the OT by the incoming ventilation air. Large number of squames are seen to be above the OT, several are surrounding the surgeons hands, above the side tables, and some are very close to the patient's knee and the surgical site. This is better visualized by the zoom-in view shown in figures 24a,b.

Figures 25, 26, and 27 show a different view angle for the squames at the same time instances as in the above discussion. It is again seen that with the blower-on several particles are lifted upwards by the thermal plumes and rise above the operating table and then are blown downwards by the incoming ventilation air.

Finally, figure 28 shows an instantaneous snapshot of squames very close to the patient's knee. It seen that several of the red-coded particles are near the bottom of the knee, whereas some yellow-coded particles are in the very close vicinity of the surgical site. Several particles are still suspended above the OT and are being transported downwards by the ventilation air and may potentially reach close to the surgical site.

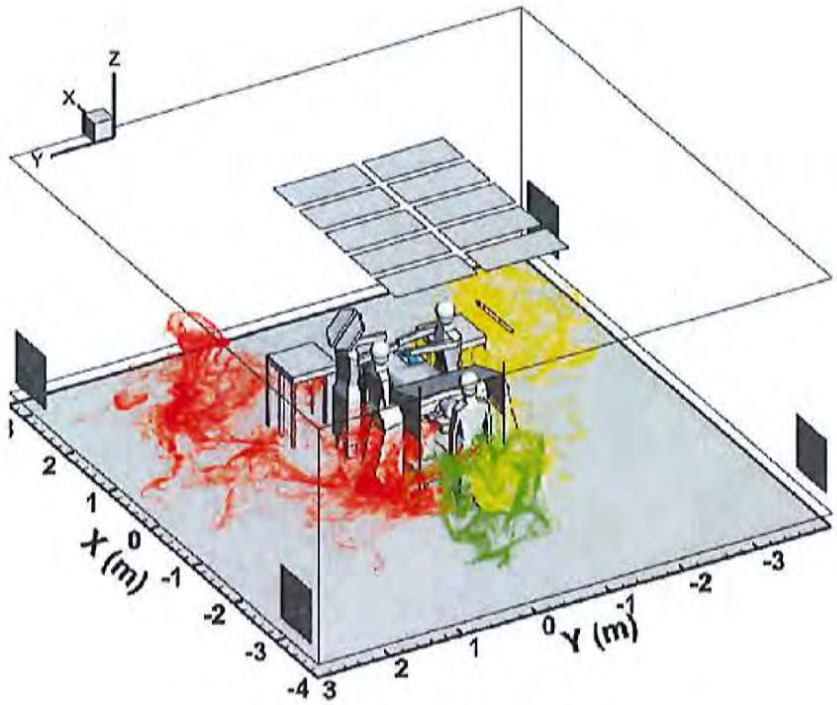


(a)

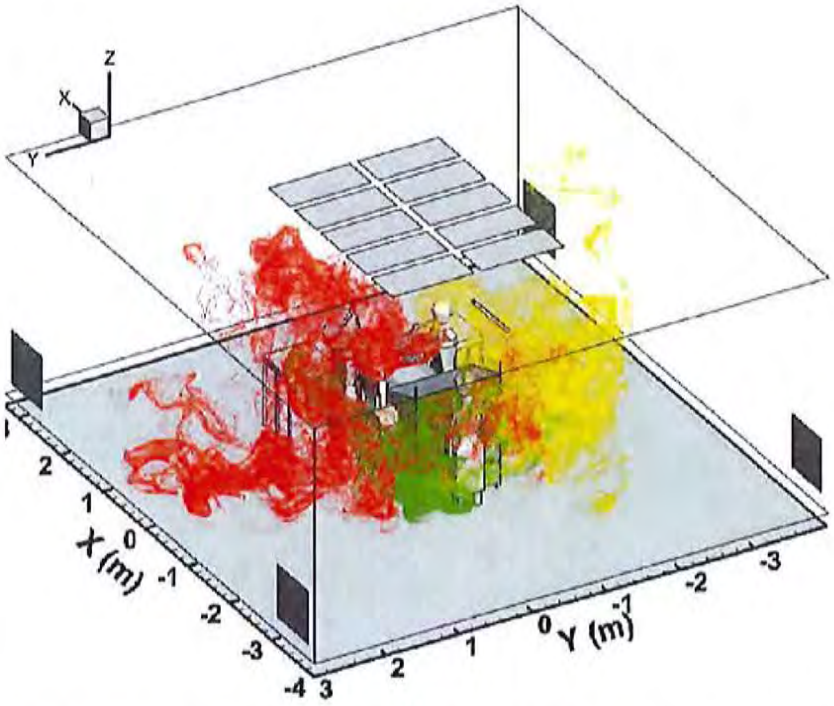


(b)

Figure 22: Instantaneous scatter plot of squames color-coded by their region of origin at 10s after initiation: (a) blower-off, (b) blower-on.

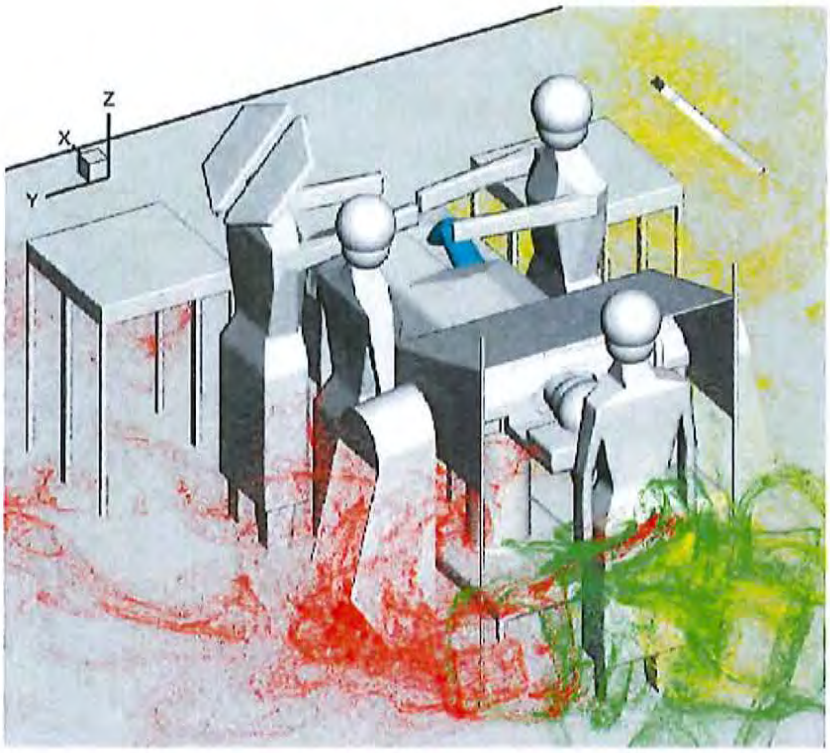


(a)

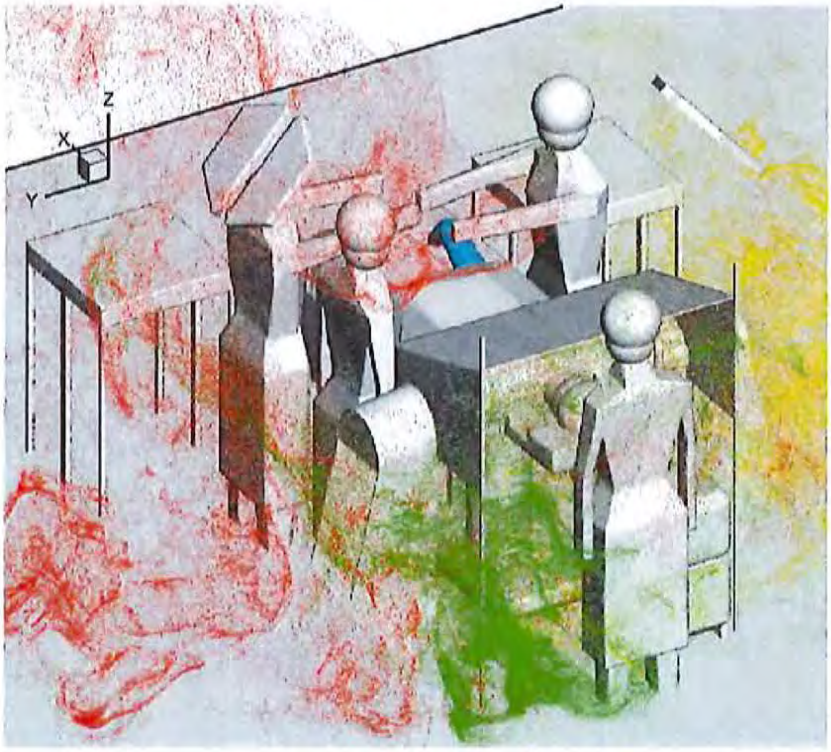


(b)

Figure 23: Instantaneous scatter plot of squames color-coded by their region of origin at 20s after initiation: (a) blower-off, (b) blower-on.

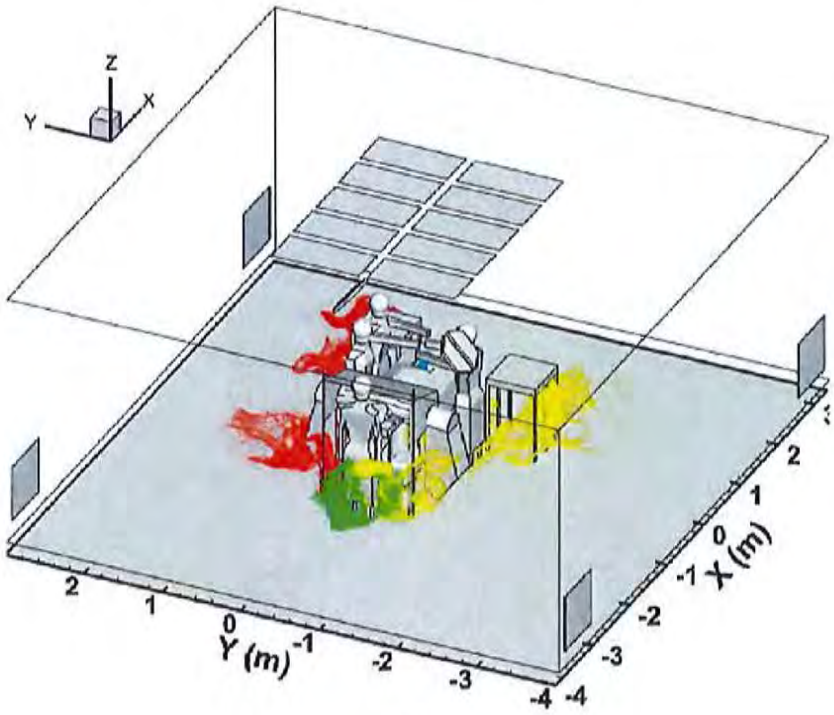


(a)

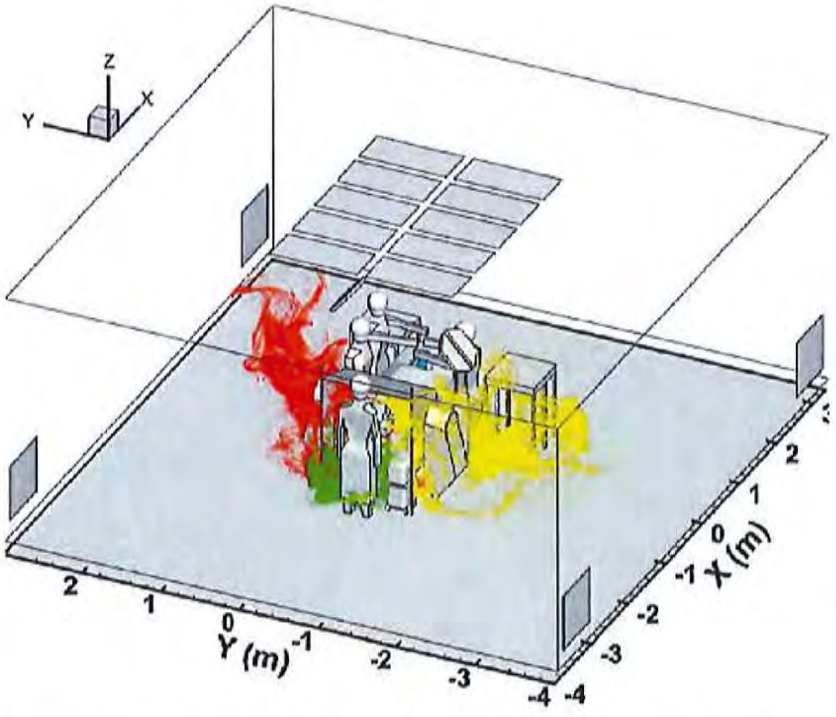


(b)

Figure 24: Zoom-in of the instantaneous scatter plot of squames color-coded by their region of origin at 20s after initiation: (a) blower-off, (b) blower-on.

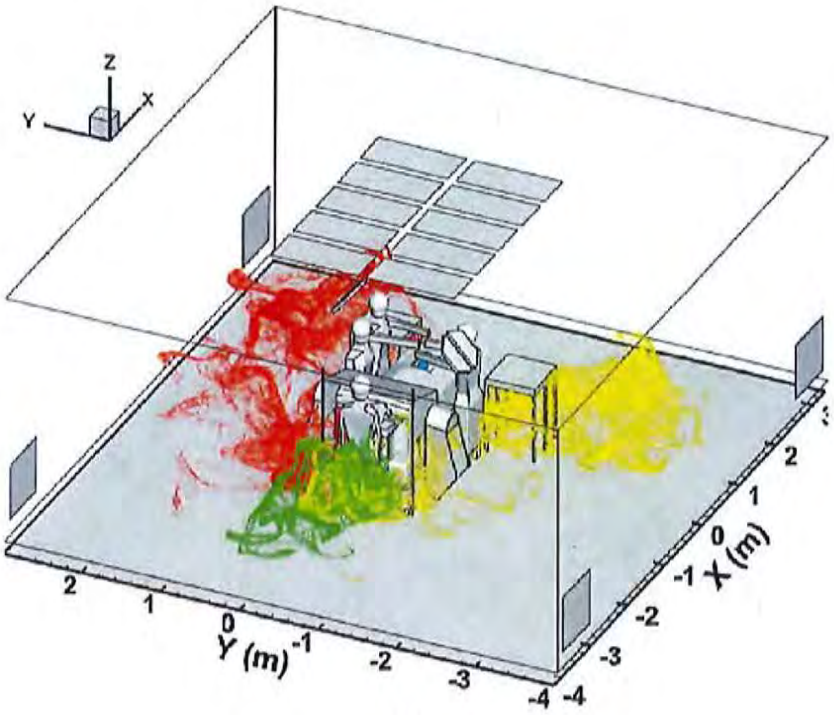


(a)

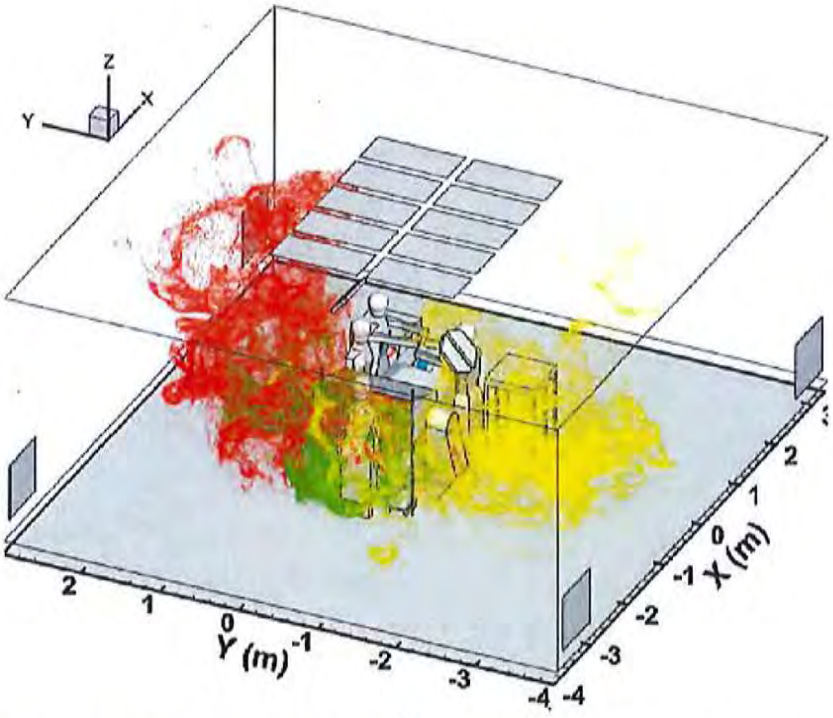


(b)

Figure 25: Instantaneous scatter plot of squames color-coded by their region of origin at 10s after initiation: (a) blower-off, (b) blower-on.

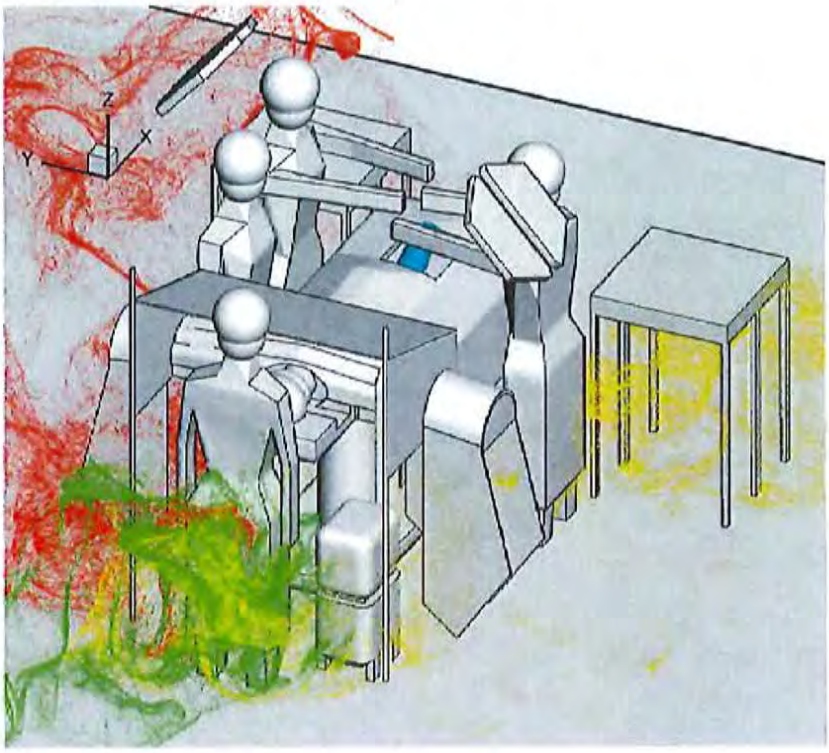


(a)

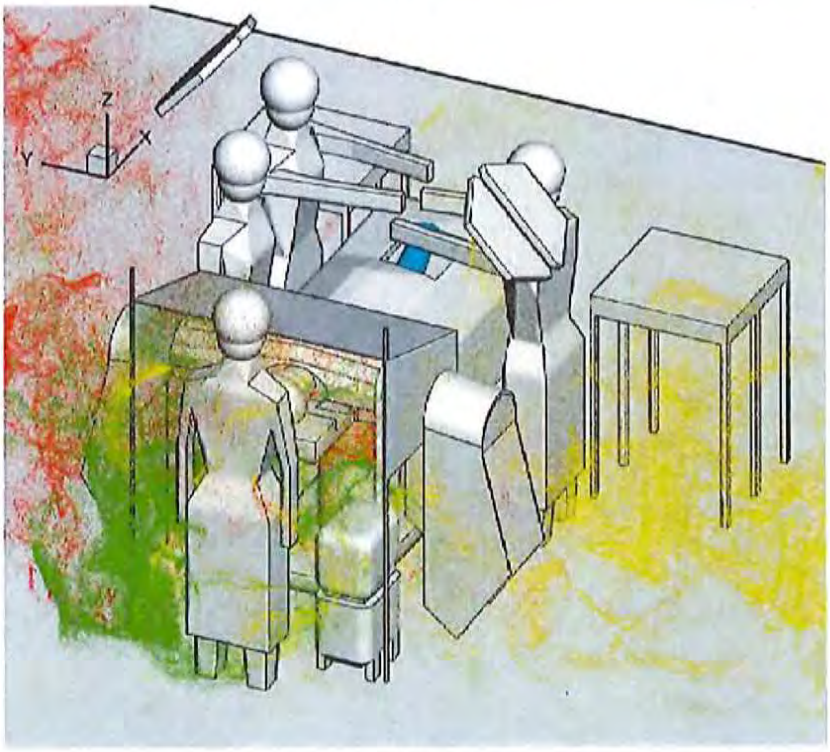


(b)

Figure 26: Instantaneous scatter plot of squames color-coded by their region of origin at 20s after initiation: (a) blower-off, (b) blower-on.



(a)



(b)

Figure 27: Zoom-in of the instantaneous scatter plot of squames color-coded by their region of origin at 20s after initiation: (a) blower-off, (b) blower-on.

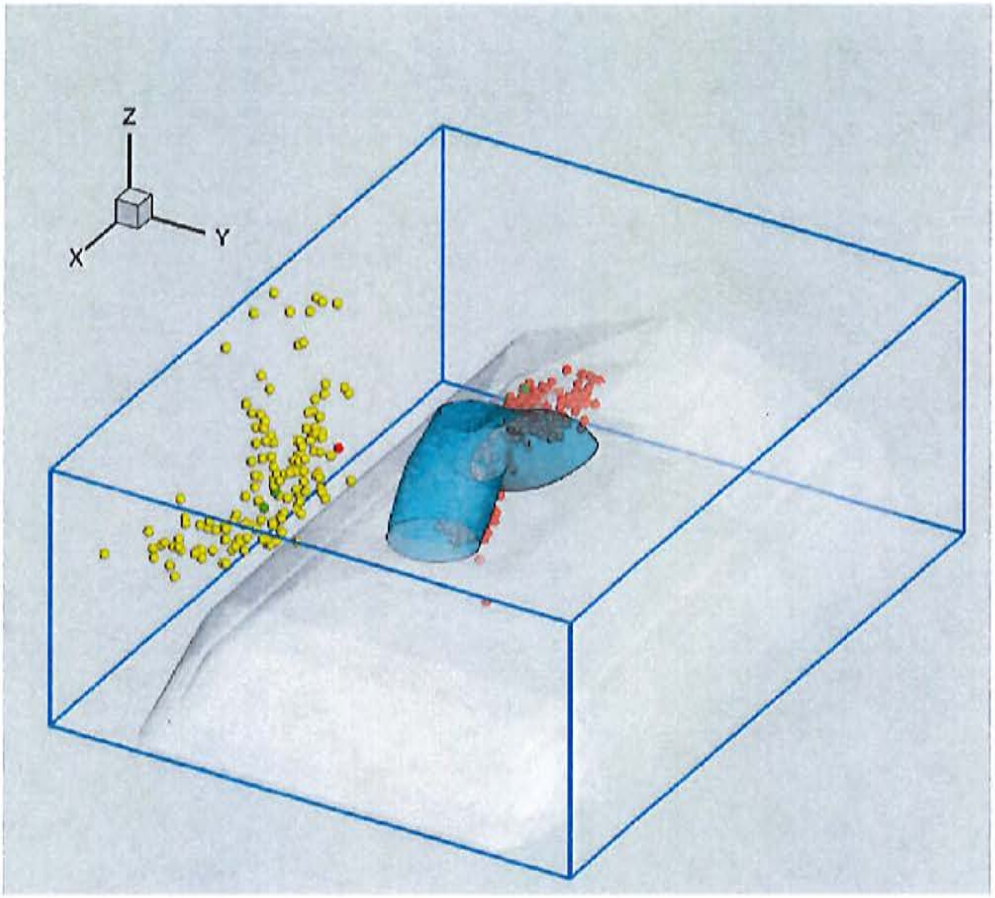


Figure 28: Zoom-in showing the instantaneous snapshot of squames near the surgical site at $t = 27$s.

4.2.3 Number density of squames in the regions of interest

To assess the probability of squames reaching the surgical site, four imaginary boxes were located as follows: two boxes covering the two side tables, a box around the OT, and a box around the patient's knee area. The surgeons and medical assistants are bound to use surgical instruments placed on the side tables. The possibility of squames reaching the surgical site is then dependent on the number density of squames within these four imaginary boxes (see figure 29). The number of squame particles inside the four boxes are recorded in time. A blue box (figure 29 (a) and (c)) is covering the whole OT. The top of this box is about 30 cm high, including the patient's whole body and the surgeons hands. An orange box (figure 29 (b) and (d)) is placed above the OT, just covering the patient's knee and part of the surgeon's hands; and the top of the box is only 2 cm above the surgeon's hands. One purple box (figure 29 (a) - (d)) is placed on each of the two side tables. The height of these boxes is about 1 cm, so that any surgical instrument placed on the side tables would be within the box.

Two computations of the trajectories of squames were performed after a statistically stationary flow field has been reached for the cases of blower-off and blower-on. Based on the average inlet air velocity and the height of the room, it takes 15 – 20s for a fluid particle to travel from the ceiling grille to the floor. First, the blower is turned off and only the ventilation air from the inlet grilles and thermal plumes created by the warm surfaces including surgical lights, surgeons' heads, patient's head, and patient's knee are responsible for the dispersion of squames. It was found that all the squames initiated in all three sections (red, green and yellow) are basically transported by the air flow reaching the floor and quickly dispersed to the for outlet grilles. After a calculation of about 25s of physical time, some squame particles do rise to the underside of the side tables, but none of the squames was found to enter the four imaginary boxes representing the regions of interest. It was concluded that without the hot air discharged from the blower, the ventilation air circulation alone cannot disperse the squames to the surgical site. The thermal plumes from various warm surfaces only slightly affect the air coming from the inlet grilles and do not affect the motion of the squames.

With the blower turned on, computations were carried out for about 30s of physical time to obtain a flow field with well established thermal plumes created by the hot air discharged from the blower. After reaching a stationary state, the squames were initiated in the same color-coded sections and the

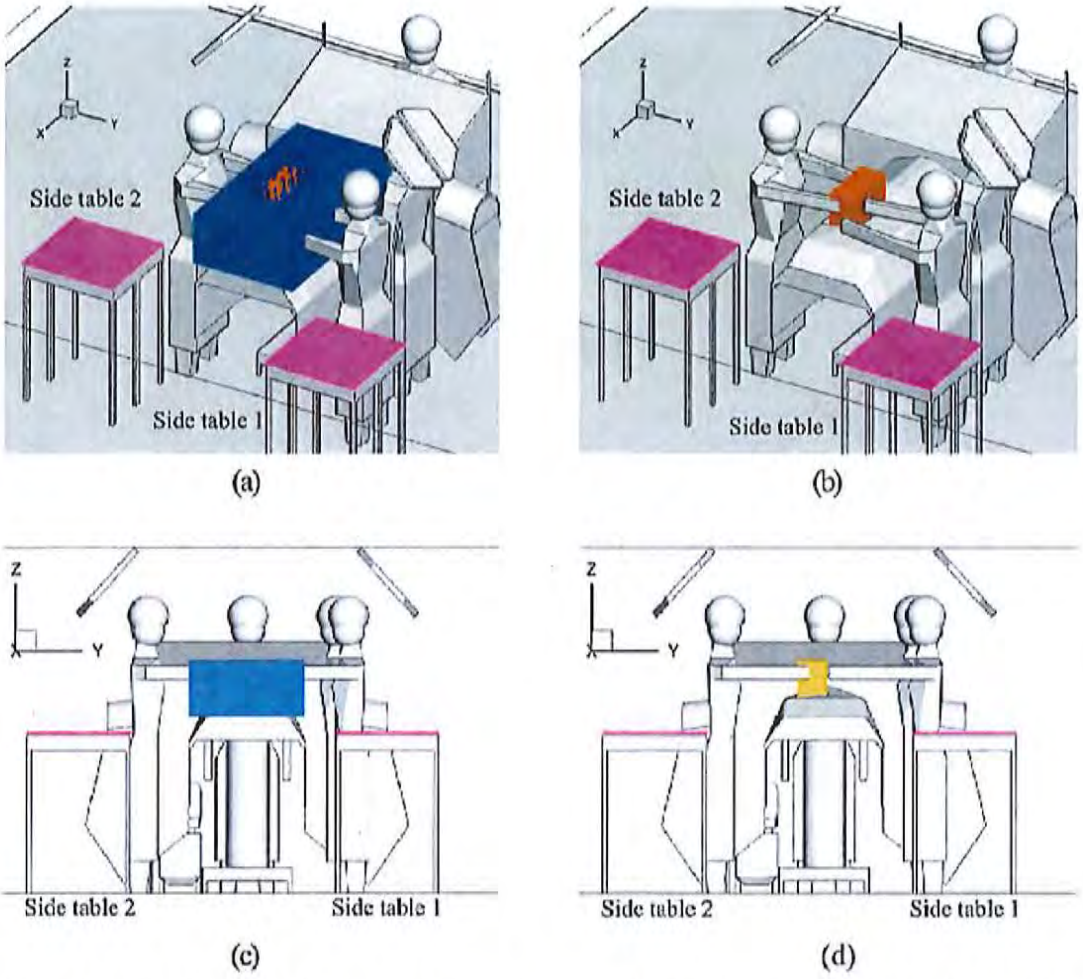
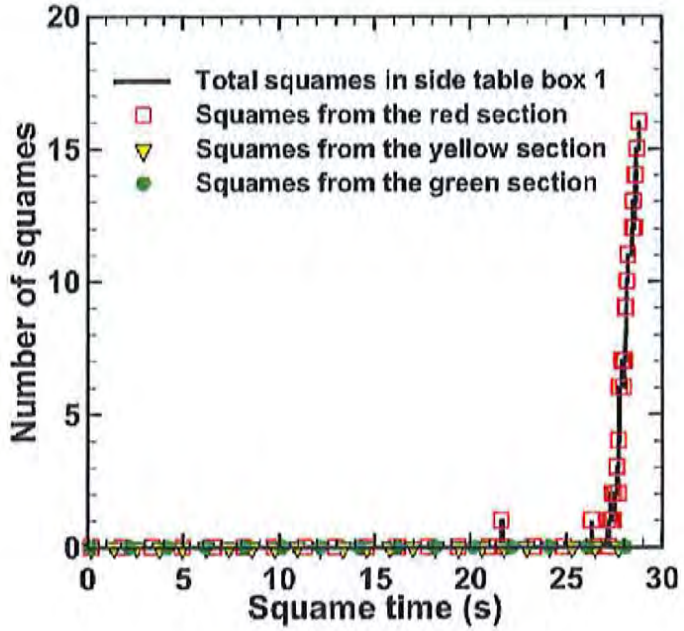


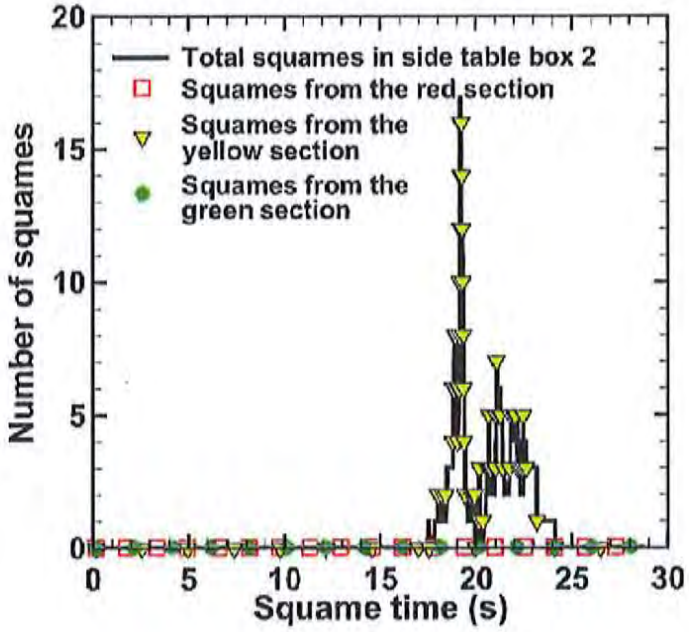
Figure 29: Four color-coded regions of interest, for recording the temporal history of the number of squames reaching them, shown in different views (a–d). The regions of interest include the zones above the two side tables, above the OT, and above the patient's knee.

computation continued for another 30s. With the blower on, hot air is discharged through the sides covering the patient's arms into the ambient air and strong thermal plumes rise under the operating table. Some of the edges of the drape are very close to the floor (see figure 4b) and the hot air plume drags squames with it making them rise upwards faster than in the case when the blower was off. A majority of the squame particles are transported away from the table towards the outlet grilles. However, a statistically significant number of particles are lifted above the operating table with some even reaching the height of the surgeons. The particles rise due to buoyancy and then get flushed down onto the operating table by the incoming ventilation air from the inlet grilles. The particles then do enter the imaginary boxes of interest, specifically above the operating table and the patient's knee.

Figures 30 and 31 show the number of squame particles as a function of time entering the four imaginary boxes of interest (above the side tables, above the operating table, and patient's knee). It can be seen from Figure 31b that no particles are found inside these boxes for the first 17s, which is about the time needed for the ventilation air to travel from the ceiling to the floor. After this time, the number of squame particles in the box above the OT increases almost in a linear fashion. Within 30s of physical time, the number of squame particles within the OT box are about 2500 and increasing. Figure 31a shows that at about 23s, some of the particles above the OT start to enter the box above the knee, which is a very narrow zone surrounding the patient's knee. The number of these particles increases linearly to about 600. Note that some of these particles do get trapped at the knee, some are carried away by the air flow and hence the number appears to be decreasing after about 25s . From the instantaneous snapshot of the squames shown in figures 24b and 27b, it can be seen that several particles are still above the OT and moving downward due to the air from the inlet grilles. It is thus expected that more particles will enter the box above the patient's knee, potentially raising the probability of infection. It is also interesting to note that the squame particles entering the box above the OT and above the knee are mainly the red-colored particles initiated from the side of the table with two surgeons. Owing to the asymmetry in the CAD model geometry, the flow pattern around each side of the table is different and the recirculation region created by the incoming air from the inlet grilles is also asymmetric. The rise and eventual trapping of the squames within the knee box is thus also related to which side of the table it originated from. The boxes above the side tables also entrain about 15 squame particles as can be seen from figures 30a,b. This suggests that

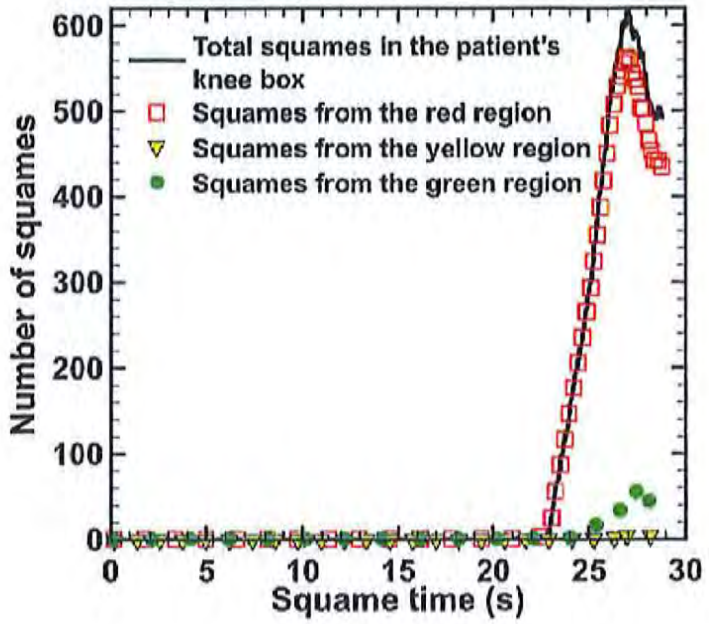


(a)

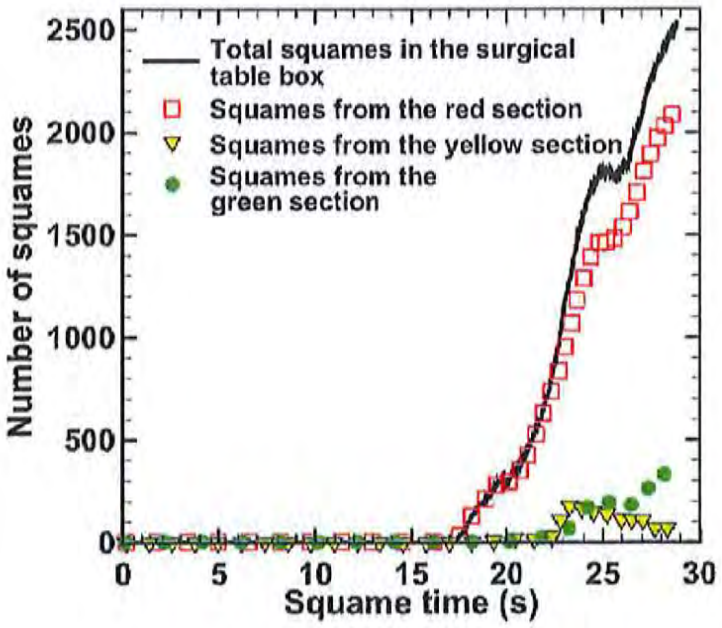


(b)

Figure 30: Temporal history of the total number of squames (shown by black color) entering four different regions of interest: (a) side table box 1, and (b) side table box 2Also shown in color is the number of color-coded squame particles entering from the red, green and yellow regions of the figure 21.



(a)



(b)

Figure 31: Temporal history of the total number of squames (shown by black color) entering four different regions of interest: (a) the patient's knee area, and (b) the OT box. Also shown in color is the number of color-coded squame particles entering from the red, green and yellow regions of the figure 21.

the surgical instruments on the side tables also have a small probability of carrying squames to the surgical site.

5 Summary and Concluding Remarks

A high-fidelity, large-eddy simulation (LES) was performed to study the interaction of the operating room (OR) ultra-clean ventilation air flow and the flow created by a forced air warming system (3M^{TM} Bair Hugger^{TM} blower) and its impact on the dispersion of squames particles. A full three-dimensional design of an OR with operating table (OT), surgical lamps, medical staff, side tables, a blower, and a patient undergoing knee surgery was constructed. Unstructured grid elements involving hexahedra, tetrahedra, pyramids and wedges were used to capture the complex geometry of the OR. An arbirary shaped, unstructured grid flow solver for LES based on governing equations for variable density in the limit of zero-Mach number was used. Ultraclean ventilation air enters the OR through 10 ceiling grilles with air changes per hour (ACH) of 24.45 and flow Reynolds number, based on the air inlet grille size and mean air inlet velocity, of 9226. The air inlet flow was developed from a periodic duct flow with the required target mass flow rate for each grille. No-slip conditions were applied for all solid surfaces and convective outflow condition was used at the four outlet grilles. Temperature values were specified at the surfaces of inlet grilles, the surgical lamps, heads of the medical staff, patient's head, and patient's knee and all other boundary surfaces were assumed adiabatic. Computations were performed on 1600 processors in parallel and flow statistics involving the time-averaged mean velocity field, turbulence intensity, and temperature distribution were computed.

Two computations were performed with the blower-off and blower-on to calculate a three-dimensional, time-dependent flow within the OR. Rising thermal plumes from the warm surfaces of surgeons heads, the patient's knee, patient's head, and the surgical lamp were calculated. With the blower on, air was drawn from the floor of the OR, heated, and blown into a blanket that covers the torso region of the patient. The blanket was covered with a plastic drape. The blower hot air generated forced convective currents and strong thermal plumes that interacted with the ultra-clean ventilation air. For both cases, trajectories of 3 million squames, placed initially on the floor in a small region surrounding the OT and surgeons, were calculated and contrasted to quantify the effect

of the hot air blower. The squames particles were assumed to be spherical in shape with 10 micron diameter and density of liquid water. The particle trajectories were tracked in a Lagrangian frame by computing the drag, lift, and buoyancy forces. The temporal variations of the number of squames particles within four imaginary boxes placed strategically above the two side tables, over the OT, and one surrounding the patient's knee were calculated and contrasted between the blower-off and blower-on cases. The following main conclusions can be drawn from these predictive computations:

1. For the case of blower-off, the ventilation air from the ceiling inlet grilles moves downwards, then is deflected by the surgical lights and the table, impinges on the floor farther away from the OT, and finally exits through the outlet grilles. Large recirculation regions are created on both sides of the table. The flow is not symmetric owing to asymmetries in the configuration of the OR contents. The maximum turbulence intensity level is about 30% in the high shear regions between the inlet air streams and the initial stagnant air in the OR, as well as near the warm surgical lights due to the buoyant plume. It is observed that the buoyant plumes from the patient's knee and other warm surfaces are relatively weak, and do not significantly alter the mean ventilation air flow.

2. For the case of blower-on, the mean flow underneath and around the OT is significantly modified and large levels of turbulence intensity are observed under the OT. The turbulence intensity levels are as high as 60% in regions affected by the rising thermal plumes from the blower. The instantaneous temperature contours confirm that the increased turbulence level is mainly because of the thermal plumes from the hot blower air causing higher temperature regions under the OT in comparison with the blower-off case. The flow is also highly asymmetric owing to the orientation and location of the drape. The rising thermal plumes are even observed to reach the ceiling in some regions and the downward ventilation flow from the inlet grilles was modified above the OT which also affected the recirculation region.

3. Drastic differences in the trajectories of the squames are observed between the blower-off and blower-on cases. With the blower-off, the majority of the squames are dispersed by the ventilation air flow towards the outlet grilles. None of the squames actually rise to the level of the side tables or the OT. In contrast, with the blower-on, a large number of squames are lifted upwards by the rising thermal plumes. Some of the squames are lifted above the surgeons

heads and are blown towards the OT by the downward moving ventilation air. Large number of squames are seen to be above the OT, several are surrounding the surgeons hands, above the side tables, and some are very close to the patient's knee and the surgical site. Majority of the squames that come close to the surgical site were found to have originated from the sides parallel to the length of the OT.

4. With the blower off, none of the squames particles were found to enter the four imaginary boxes placed above the side tables, OT, and a region surrounding the patient's knee. Some particles are lifted from the floor over time, but none rise close to the level of the imaginary boxes as the downward flow due to the ventilation air keeps the particles closer to the floor. With the blower turned on, hot air discharged from the edges of the drape and the resultant thermal plumes drag the squames, making them rise upwards. Some of the squames rise above the surgeons heads in the recirculation region on the sides of the OT. These particles are then flushed down onto the OT by the ventilation air from the inlet grilles. Statistically significant particles do enter the imaginary boxes of interest above the operating table and the patient's knee. Few particles are also observed above the side tables.

Starting with the worst-case scenario of having squames on the floor, it was shown that the hot air from the blower and the resultant thermal plumes are capable of lifting the particles and transporting them to the side tables, above the operating table, and the surgical site. It should be emphasized that if we also include the repetitive motion of the surgeons, the motion of medical assistants to fetch the surgical instruments placed on the side tables, and the resulting suspended squames shed by all staff in the OR, then the probability of dispersing the squames to the surgical site will be increased even further.

Although computationally intensive, large-eddy simulation of convective ventilation air flow and hot air from the blower in an OR is necessary to provide reliable predictions of the turbulent flow and dispersion of squames.

Appendix A

The aerodynamic behavior of squames suspended in a fluid is in general dependent upon the size and shape of the squames, their density, relative velocity with respect to the fluid motion, and density of the fluid. In the present study, the squames are suspended in air at room temperature (density ρ_g). The human skin cells or squames typically are disc-shaped with a diameter ranging from 4–20μm and a thickness of 3–5μm with density close to that of liquid water ($\rho_p = 1000\text{kg/m}^3$) (Noble *et al.*, 1963; Noble, 1975; Snyder, 2009).

Settling of a squame particle depends on its weight, the drag and buoyancy force on the particle, and its orientation relative to the flow direction. Owing to the changes in orientation and also resultant rotation and torque on disc particles, computing large number of trajectories in a Lagrangian frame is complicated. It is thus easier to assume these particles of spherical shape with an equivalent diameter such that their aerodynamic characteristics are matched. An equivalent diameter of the spherical particle should be calculated by matching the settling velocities for the two shapes.

Since $\rho_p/\rho_g = 1000$, the buoyancy force is much smaller compared to the weight of the particle. Then the settling velocity can be obtained from the balance of drag and gravitational forces,

$$F_d = F_g. \tag{24}$$

The drag and gravitational forces on a disc-shaped particle are given as,

$$F_d = C_{d,\text{disc}} \frac{1}{2} \rho_g U_{\text{disc}}^2 A_p, \tag{25}$$

$$F_g = (A_p h_{\text{disc}}) \rho_p \text{g}; \; A_p = \frac{\pi}{4} D_{p,\text{disc}}^2 \tag{26}$$

where U_{disc} is the settling velocity of the disc, $C_{d,disc}$ is the drag coefficient, A_p is the frontal area of the circular disc, g is the gravitational acceleration, $D_{p,\text{disc}}$ is the diameter, and h_{disc} is the thickness of the disc. Equating the drag force to the weight of the disc to obtain the settling velocity as,

$$U_{\text{disc}} = \sqrt{2\text{g} \left(\frac{\rho_p}{\rho_g} \right) \left(\frac{h_{\text{disc}}}{C_{d,\text{disc}}} \right)}. \tag{27}$$

Following similar procedure, the settling velocity of a sphere of diameter $D_{p,\text{sphere}}$ can be ob-

tained as,

$$U_{\text{sphere}} = \sqrt{\frac{4}{3} g \left(\frac{\rho_p}{\rho_g}\right) \left(\frac{D_{p,\text{sphere}}}{C_{d,\text{sphere}}}\right)}, \tag{28}$$

where $C_{d,\text{sphere}}$ is the drag coefficient on a spherical particle.

In order to match the aerodynamic performance of the two shapes, the two settling velocities should be the same. Equating U_{disc} and U_{sphere} we get,

$$D_{p,\text{sphere}} = \frac{3}{2} h_{\text{disc}} \left(\frac{C_{d,\text{sphere}}}{C_{d,\text{disc}}}\right). \tag{29}$$

For Stokes flow ($Re \leq 1$), the drag coefficients are given as (Munson *et al.*, 1990),

$$C_{d,\text{sphere}} = \frac{24}{Re} \tag{30}$$

$$C_{d,\text{disc}} = \frac{20.4}{Re}, \quad \text{flow normal to circular disc} \tag{31}$$

$$= \frac{13.6}{Re}, \quad \text{flow parallel to circular disc.} \tag{32}$$

Using a disc thickness of $h_{\text{disc}} = 5\mu\text{m}$, and using the drag coefficients for the disc and the sphere, equation (29) gives an equivalent spherical diameter in the range of $D_{p,sphere} = 8.78$ and $13.2\mu\text{m}$. Thus, an assumption of 10 micron spherical particle is reasonable to obtain similar dispersion behavior on an average as that of the disc-shaped squames particles.

References

ALBRECHT, MARK, GAUTHIER, ROBERT L, BELANI, KUMAR, LITCHY, MARK & LEAPER, DAVID 2011 Forced-air warming blowers: An evaluation of filtration adequacy and airborne contamination emissions in the operating room. *American journal of infection control* **39** (4), 321–328.

APTE, SV, GOROKHOVSKI, M. & MOIN, P. 2003*a* LES of atomizing spray with stochastic modeling of secondary breakup. *International Journal of Multiphase Flow* **29** (9), 1503–1522.

APTE, SV, MAHESH, K. & LUNDGREN, T. 2008*a* Accounting for finite-size effects in simulations of disperse particle-laden flows. *International Journal of Multiphase Flow* **34** (3), 260–271.

APTE, SV, MAHESH, K. & MOIN, P. 2008*b* Large–eddy simulation of evaporating spray in a coaxial combustor. *Proceedings of the Combustion Institute* **32**, accepted for publication.

APTE, SV, MAHESH, K., MOIN, P. & OEFELEIN, JC 2003*b* Large-eddy simulation of swirling particle-laden flows in a coaxial-jet combustor. *International Journal of Multiphase Flow* **29** (8), 1311–1331.

APTE, SOURABH V, MAHESH, KRISHNAN, GOROKHOVSKI, MICHAEL & MOIN, PARVIZ 2009 Stochastic modeling of atomizing spray in a complex swirl injector using large eddy simulation. *Proceedings of the Combustion Institute* **32** (2), 2257–2266.

AUSTIN, PAUL N 2015 Guest editorial. *AANA journal* **83** (4), 237.

CHEN, X-Q & PEREIRA, JCF 1998 Computation of particle dispersion in turbulent liquid flows using an efficient lagrangian trajectory model. *International journal for numerical methods in fluids* **26** (3), 345–364.

CHOW, TIN-TAI & WANG, JINLIANG 2012 Dynamic simulation on impact of surgeon bending movement on bacteria-carrying particles distribution in operating theatre. *Building and Environment* **57**, 68–80.

CLARK, RAYMOND P. & DE CALCINA-GOFF, MERVYN L. 2009 Some aspects of the airborne transmission of infection. *Journal of The Royal Society Interface* **6** (Suppl 6), S767–S782.

CROWE, CT, TROUTT, TR & CHUNG, JN 1996 Numerical models for two-phase turbulent flows. *Annual Review of Fluid Mechanics* **28** (1), 11–43.

DRUZHININ, OA & ELGHOBASHI, S. 1998 Direct numerical simulations of bubble-laden turbulent flows using the two-fluid formulation. *Physics of Fluids* **10**, 685.

EATON, JK & FESSLER, JR 1994 Preferential concentration of particles by turbulence. *International Journal of Multiphase Flow* **20**, 169–209.

EATON, J.K. & SEGURA, J.C. 2006 On momentum coupling methods for calculation of turbulence attenuation in dilute particle-laden gas flows. *Fluid Mechanics and its Applications* **81**, 39.

ELGHOBASHI, S. 1994 On predicting particle-laden turbulent flows. *Flow, Turbulence and Combustion* **52** (4), 309–329.

ELGHOBASHI, S. 2006 An updated classification map of particle-laden turbulent flows. *Fluid Mechanics and Its Applications* **81**, 3–10.

FERRANTE, A. & ELGHOBASHI, S. 2004 On the physical mechanisms of drag reduction in a spatially developing turbulent boundary layer laden with microbubbles. *Journal of Fluid Mechanics* **503**, 345–355.

FERRANTE, A. & ELGHOBASHI, S. 2007 On the accuracy of the two-fluid formulation in direct numerical simulation of bubble-laden turbulent boundary layers. *Physics of Fluids* **19**, 045105.

GERMANO, MASSIMO, PIOMELLI, UGO, MOIN, PARVIZ & CABOT, WILLIAM H 1991 A dynamic subgrid-scale eddy viscosity model. *Physics of Fluids A: Fluid Dynamics (1989-1993)* **3** (7), 1760–1765.

HAM, F., APTE, S., IACCARINO, G., WU, X., HERRMANN, M., CONSTANTINESCU, G., MAHESH, K. & MOIN, P. 2003 Unstructured LES of reacting multiphase flows in realistic gas turbine combustors. Annual Research Briefs 2003. *Center for Turbulence Research, NASA Ames/Stanford Univ* pp. 139–160.

HAM, FRANK & IACCARINO, GIANLUCA 2004 Energy conservation in collocated discretization schemes on unstructured meshes. *Annual Research Briefs* **2004**, 3–14.

912 KELLAM, MELISSA D, DIECKMANN, LORAINE S & AUSTIN, PAUL N 2013 Forced-air warming
913 devices and the risk of surgical site infections. *AORN journal* **98** (4), 353–369.

914 KRAVCHENKO, AG & MOIN, PARVIZ 1997 On the effect of numerical errors in large eddy simu-
915 lations of turbulent flows. *Journal of Computational Physics* **131** (2), 310–322.

916 KULICK, JD, FESSLER, JR & EATON, JK 2006 Particle response and turbulence modification in
917 fully developed channel flow. *Journal of Fluid Mechanics Digital Archive* **277**, 109–134.

918 LEAPER, DAVID, ALBRECHT, MARK & GAUTHIER, ROBERT 2009 Forced-air warming: a source
919 of airborne contamination in the operating room? *Orthopedic reviews* **1** (2), 28.

920 LEES, JULIENNE & BRIGHTON, WD 1972 Simulated human skin scales. *Journal of Hygiene*
921 **70** (03), 557–565.

922 LEGG, AJ, CANNON, T & HAMER, AJ 2012 Do forced air patient-warming devices disrupt unidi-
923 rectional downward airflow? *J Bone Joint Surg Br* **94** (2), 254–256.

924 MAHESH, K., CONSTANTINESCU, G., APTE, S., IACCARINO, G., HAM, F. & MOIN, P. 2006
925 Large-eddy simulation of reacting turbulent flows in complex geometries. *Journal of Applied*
926 *Mechanics* **73**, 374.

927 MAHESH, K., CONSTANTINESCU, G. & MOIN, P. 2004 A numerical method for large-eddy sim-
928 ulation in complex geometries. *Journal of Computational Physics* **197** (1), 215–240.

929 MAXEY, MARTIN R & RILEY, JAMES J 1983 Equation of motion for a small rigid sphere in a
930 nonuniform flow. *Physics of Fluids (1958-1988)* **26** (4), 883–889.

931 MCGOVERN, PD, ALBRECHT, M, BELANI, KG, NACHTSHEIM, C, PARTINGTON, PF, CAR-
932 LUKE, I & REED, MR 2011 Forced-air warming and ultra-clean ventilation do not mix. *J Bone*
933 *Joint Surg Br* **93** (11), 1537–1544.

934 MCNEILL, JAMES, HERTZBERG, JEAN & ZHAI, ZHIQIANG JOHN 2013 Experimental investiga-
935 tion of operating room air distribution in a full-scale laboratory chamber using particle image
936 velocimetry and flow visualization .

937 MCNEILL, JAMES S *et al.* 2012 Field measurements of thermal conditions during surgical proce-
938 dures for the development of cfd boundary conditions. *ASHRAE Transactions* **118**, 596.

939 MEMARZADEH, FARHAD 2003 Reducing risks of surgery. *ASHRAE journal* **45** (2), 28.

940 MEMARZADEH, FARHAD & MANNING, ANDREW P 2002 Comparison of operating room ventila-
941 tion systems in the protection of the surgical site/discussion. *ASHRAE transactions* **108**, 3.

942 MITTAL, RAJAT & MOIN, PARVIZ 1997 Suitability of upwind-biased finite difference schemes for
943 large-eddy simulation of turbulent flows. *AIAA journal* **35** (8), 1415–1417.

944 MOIN, P. & APTE, SV 2006 Large-eddy simulation of realistic gas turbine combustors. *AIAA Jour-*
945 *nal* **44** (4), 698–708.

946 MOIN, P. & MAHESH, K. 1998 Direct numerical simulation: A tool in turbulence research. *Annual*
947 *Reviews in Fluid Mechanics* **30** (1), 539–578.

948 MOIN, P., SQUIRES, K., CABOT, W. & LEE, S. 1991 A dynamic subgrid model for compressible
949 turbulence and scalar transport. *Physics of Fluids A.* **3**, 2746–2757.

950 MORETTI, B, LAROCCA, AMV, NAPOLI, C, MARTINELLI, D, PAOLILLO, L, CASSANO, M,
951 NOTARNICOLA, A, MORETTI, L & PESCE, V 2009 Active warming systems to maintain pe-
952 rioperative normothermia in hip replacement surgery: a therapeutic aid or a vector of infection?
953 *Journal of Hospital Infection* **73** (1), 58–63.

954 MUNSON, BRUCE ROY, YOUNG, DONALD F & OKIISHI, THEODORE H 1990 Fundamentals of
955 fluid mechanics. *New York* **3** (4).

956 NG, V, LAI, A & HO, V 2006 Comparison of forced-air warming and electric heating pad for
957 maintenance of body temperature during total knee replacement. *Anaesthesia* **61** (11), 1100–1104.

958 NOBLE, WC 1975 Dispersal of skin microorganisms. *British Journal of Dermatology* **93** (4), 477–
959 485.

960 NOBLE, WC, LIDWELL, OM, KINGSTON, D *et al.* 1963 The size distribution of airborne particles
961 carrying micro-organisms. *J Hyg (Lond)* **61** (385), e391.

962 PEREIRA, MARCELO LUIZ & TRIBESS, ARLINDO 2005 A review of air distribution patterns in
963 surgery rooms under infection control focus. *Revista de Engenharia Térmica* **4** (2).

964 PIERCE, C.D. & MOIN, P. 1998*a* Turbulent flow over three-dimensional dunes: 2. Fluid and bed
965 stresses. *Physics of Fluids* **10**, 3041–3044.

966 PIERCE, CHARLES DAVID 2001 Progress-variable approach for large-eddy simulation of turbulent
967 combustion. PhD thesis, Citeseer.

968 PIERCE, CHARLES D & MOIN, PARVIZ 1998*b* Large eddy simulation of a confined coaxial jet with
969 swirl and heat release. *AIAA paper* **2892**.

970 PIOMELLI, U 2014 Large eddy simulations in 2030 and beyond. *Philosophical Transactions of*
971 *the Royal Society of London A: Mathematical, Physical and Engineering Sciences* **372** (2022),
972 20130320.

973 POPE, SB 2000 *Turbulent Flows*. Cambridge University Press.

974 POZORSKI, JACEK & APTE, SOURABH V 2009 Filtered particle tracking in isotropic turbulence
975 and stochastic modeling of subgrid-scale dispersion. *International Journal of Multiphase Flow*
976 **35** (2), 118–128.

977 READE, W.C. & COLLINS, L.R. 2000 Effect of preferential concentration on turbulent collision
978 rates. *Physics of Fluids* **12**, 2530.

979 ROUSON, D.W.I. & EATON, J.K. 2001 On the preferential concentration of solid particles in tur-
980 bulent channel flow. *Journal of Fluid Mechanics* **428**, 149–169.

981 SAARINEN, PEKKA E, KALLIOMÄKI, PETRI, TANG, JULIAN W & KOSKELA, HANNU 2015
982 Large eddy simulation of air escape through a hospital isolation room single hinged doorwayval-
983 idation by using tracer gases and simulated smoke videos. *PloS one* **10** (7), e0130667.

984 SAFFMAN, PGT 1965 The lift on a small sphere in a slow shear flow. *Journal of fluid mechanics*
985 **22** (02), 385–400.

986 SESSLER, DANIEL I, OLMSTED, RUSSELL N & KUELPMANN, RUEDIGER 2011 Forced-air warm-
987 ing does not worsen air quality in laminar flow operating rooms. *Anesthesia & Analgesia* **113** (6),
988 1416–1421.

989 SNYDER, OP 2009 A 'Safe Hands' hand wash program for retail food operations: a technical
990 review. *Yeast* **55** (18.5), 14–8.

991 SOMMERFELD, M, ANDO, A & WENNERBERG, D 1992 Swirling, particle-laden flows through a
992 pipe expansion. *Journal of fluids engineering* **114** (4), 648–656.

993 SRIDHAR, G. & KATZ, J. 1999 Effect of entrained bubbles on the structure of vortex rings. *J. Fluid*
994 *Mech.* **397** (-1), 171–202.

995 STRAUB, A. 2016 *Bentley Microstation Design V8i, M/E Engineering, P.C.*. 150 North Chestnut
996 Street, Rochester, NY 14604, www.meengineering.com.

997 TENNEKES, HENDRIK & LUMLEY, JOHN LEASK 1972 *A first course in turbulence*. MIT press.

998 WARTTIG, SHERYL, ALDERSON, PHIL, CAMPBELL, GILLIAN & SMITH, ANDREW F 2014 Inter-
999 ventions for treating inadvertent postoperative hypothermia. *The Cochrane Library* .

1000 WOOD, AM, MOSS, C, KEENAN, A, REED, MR & LEAPER, DAVID J 2014 Infection control
1001 hazards associated with the use of forced-air warming in operating theatres. *Journal of Hospital*
1002 *Infection* **88** (3), 132–140.

Exhibit 2

Summary of Opinions

I have conducted a computation fluid dynamic simulation of a typical operating room and knee implant surgery procedure. In creating the three-dimensional model of the operating room and its setup, many assumptions were made to reduce the effects of the Bair Hugger patient warming system on disrupting the ventilation air flow. For example, the HVAC system modeled is superior to many, if not all, the HVAC systems used in operating rooms. Similarly, the assumptions made for draping, particle count, position of lights, etc. are all in favor of reducing the disruption caused by the Bair Hugger patient warming system.

Based upon my education, training, experience, and the computation fluid dynamics analysis discussed in Exhibit A, I will offer the following general causation opinions within a reasonable degree of engineering certainty:

1. The use of a Bair Hugger Model 750 Blower with the Bair Hugger Upper Body blanket disrupts the turbulent airflow around the operating table.

2. The use of a Bair Hugger Model 750 Blower with the Bair Hugger Upper Body blanket significantly increases the particle count over the surgical site, operating table, and side tables.

3. The use of a Bair Hugger Model 750 Blower with the Bair Hugger Upper Body blanket significantly reduces the effect of the operating room's HVAC system in protecting the surgical site from contaminants.

4. The use of a Bair Hugger Model 505 Blower with the Bair Hugger Upper Body blanket will have the same effects as stated in items 1 through 3 above, but at a reduced temporal rate, i.e. it would take longer time to observe the same effects of BH Model 750.

5. The Bair Hugger patient warming system significantly increases the number of contaminants reaching the operating table.

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M.Sc. (Mechanical Engineering)	1971	Univ. of Southern California, Los Angeles, USA.
Ph.D. (Mechanical Engineering)	1974	Imperial College, University of London, England.
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Professional Activities (partial list)

Member of the National Academy of Engineering.
Fellow of the American Physical Society.
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Visiting Fellow of Cambridge University, Wolfson College, England, 1999.
Senior Award of International Conference on Multiphase Flow, Florence, Italy, May 25, 2016.
Chair of the Nominating Committee of American Physical Society, Div. Fluid Dynamics (2014-2015).
Member of Fellowship Committee of American Physical Society, Div. Fluid Dynamics (2009-11).
Member of Science and Engineering Advisory Committee (SETAC) of Blue Waters supercomputer project(2016-2017). https://bluewaters.ncsa.illinois.edu/setac
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Member of the Combustion Institute.
Member of EuroMech.
Member of the Editorial Advisory Board of International J. of Multiphase Flow(2010-present).
Guest Editor of International J. of Multiphase Flow, Special Issue on Point-particle model for disperse turbulent flows, vol. 35, 2009.
DIC: Diploma of Membership of Imperial College in Mech. Engineering, 1974.
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Major Research Interests

Direct numerical simulation of turbulent flows, including multiphase and chemaically-reacting flows, and biomedical flows.

Research and Professional Experience

March 2015 -Present **UC Distinguished Professor**, Mechanical and Aerospace Engineering Department, University of California, Irvine.

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July 1997 - June 2002 **Chairman**, Mechanical and Aerospace Engineering Department, University of California, Irvine.
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Physics of Fluids
Nature
Science
Physical review Letters
International Journal of Multiphase Flow
Journal of Combustion Science and Technology
Combustion and Flame
Journal of American Institute of Aeronautics and Astronautics
Journal of Fluids Engineering
Journal of Heat Transfer
International Journal of Numerical Heat Transfer
International Journal of Heat and Mass Transfer
International Journal of Heat and Fluid Flow
Progress in Energy and Combustion Science
Journal of Applied Mathematical Modeling
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Consulting

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Ballistic Missile Advance Technology Center
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1981 - 1996
Jet Propulsion Laboratory
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Invited Keynote and Distinguished Lectures since 2000

L1. Elghobashi, S. " On the two-fluid and trajectory approaches for DNS of turbulent particle-laden flows", Part 1: DNS of bubble-laden flows via the two-fluid approach, [**Invited Lecture**] Von Karman Institute for Fluid Dynamics, Rhode-Saint-Genese, **Belgium**, April 3-7, 2000.

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L3. Elghobashi, S. " On the point-force approximation in DNS of prticle-laden turbulent flows with two-way coupling", **[Invited lecture]** ERCOFTAC Conference on Dynamics of Particle-Laden Flows, Zurich, **Switzerland**, July 3-5, 2000.

L4. L4. Elghobashi, S. "Recent Advance in DNS of Particle-Laden Turbulent Flows" **[Invited Plenary lecture]**, XI Congress on Numerical Methods and their Applications, ENIEF 2000 , San Carlos de Bariloche, **Argentina**, November 20-24, 2000.

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L8. S. Elghobashi " Reynolds number effect on drag reduction in a microbubble-laden spatially-developing turb. boundary layer", **Euromech Conference on Hydrodynamics of bubbly flows- [Invited Lecture]**- Lorentz Center, Leiden, **the Netherlands,** June 6-8, 2005.

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L11. S. Elghobashi " Reynolds number effect on drag reduction in a microbubble-laden spatially-developing turb. boundary layer", **Thirteen IUTAM Advanced School & Workshop, Particle Dispersion in Turbulent Flows, [Invited Lecture II]**- CISM, Udine, **Italy,** September 12-16, 2005.

L12. S. Elghobashi, " Direct simulation of turbulent flows laden with particles or bubbles", CIEMAT : Research Centre for Energy, Environment and Technology, **[Invited Lecture]**, Madrid, **Spain,** June 21, 2006.

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L16. S. Elghobashi " The physical mechanisms of two-way interactions between dispersed particles and turbulent flows", **Workshop on Clouds and Turbulence Institute for Mathematical Sciences,** Imperial College, **[Invited Lecture]**, London, **England,** March 23-25, 2009.

L17. S. Elghobashi " How do inertial particles modify isotropic turbulence ?" **International Workshop- Solving the Riddle of Turbulence: What, Why, and How?** Max Planck Institute for Dynamics and Self-Organization, **[Invited Lecture]**, Göttingen, **Germany,** May 6 - May 9, 2009.

L18. S. Elghobashi "How do inertial particles modify isotropic turbulence ?" **International Symposium on Turbulence",** **[Invited Lecture]**, Peking University, **Beijing, China,** Sept. 21-25, 2009.

L19. S. Elghobashi "How do inertial particles modify isotropic turbulence ?" **4th Latin-American Workshop on CFD ", [Keynote Lecture], Rio de Janiero, Brazil,** July 11-14, 2010.

L20. S. Elghobashi "On turbulence modulation by dispersed inertial particles"
13th European Turbulence Conference, ETC 13, [Keynote Lecture] University of Warsaw, Poland, September 12-15, 2011.

L21. F. Lucci, V.S. Lvov, A. Ferrante and S. Elghobashi, "Eulerian-Lagrangian bridge for the energy and dissipation spectra in homogeneous turbulence", **[Invited Lecture]**, International Workshop on "Lagrange versus Euler for turbulent flows",
Wolfgang Pauli Institute, Vienna, Austria, May 7-12, 2012.

L22. S. Elghobashi "On the multi-way interactions between turbulent flows and suspended sediment"
International symposium on two-phase modeling for sediment dynamics in geophysical flows(THESIS-2013) [Keynote Lecture] Chatou, Paris, France, June 10-12, 2013.

L23. S. Elghobashi "On the multi-way interactions between turbulent flows and suspended particles"
Fluid-Mediated Particle Transport in Geophysical Flows (GEOFLOWS13), Kavli Institute for Theoretical Physics [Invited Lecture] UCSB, Santa Barbara, California, December 10, 2013.

L24. S. Elghobashi " Modulation of isotropic turbulence by dispersed particles," **Huazhong University of Science and Technology, Wuhan, China,** June 9, 2014. **[Plenary Lecture].**

L25. S. Elghobashi "Homogeneous shear turbulence modulation by dispersed small

particles," **Huazhong University of Science and Technology, Wuhan, China,** June 10, 2014. [**keynote Lecture**].

L26. S. Elghobashi "Modulation of isotropic turbulence by finite-size particles," **Huazhong University of Science and Technology, Wuhan, China,** June 11, 2014. [**keynote Lecture**].

L27. S. Elghobashi "How do dispersed inertial particles modify turbulent flows," Department of Mechanics and Engineering Science, **Peking University, China,** June 17, 2014 . [**Distinguished lecture**].

L28. S. Elghobashi "How do dispersed inertial particles modify turbulent flows," Center for Turbulence Research, **Stanford University,** July 25, 2014. [**Distinguished lecture**].

L29. S. Elghobashi "How do dispersed inertial particles modify turbulent flows," Computational and Applied Mathematics, **Pennsylvania State University,** October 10, 2014. [**Distinguished lecture**].

L30. S. Elghobashi "How do dispersed inertial particles modify turbulent flows," Aerospace Engineering department, **University of Minnesota,** April 21, 2015. [**Distinguished lecture**].

L31. S. Elghobashi "How do dispersed inertial particles modify turbulent flows," Mechanical Engineering department, **Northwestern University,** February 1, 2016. [**Distinguished lecture**].

L32. S. Elghobashi "How do dispersed inertial particles modify turbulent flows," Mechanical Engineering department, **MIT,** February 3, 2016. [**Distinguished lecture**].

Publications

Articles in Books

B1 Elghobashi, S.E., "Studies in the Prediction of Turbulent Diffusion Flames", **Studies in Convection**, Vol. 2, B.E. Launder, ed., Academic Press, London, (1977).

B2 Elghobashi, S. E.,and Nomura, K.N., "Direct Simulation of a Passive Diffusion Flame in Sheared and Unsheared Homogeneous Turbulence", **Turbulent Shear Flows 7** , pp. 313-329, W.C. Reynolds, ed., Springer-Verlag , (1991).

B3 Elghobashi, S. E. "Direct Simulation of turbulent flows laden with dispersed particles ", **Handbook on Multiphase Flow** , pp. 13-34:13-60, C. Crowe, ed., CRC , (2005).

B4 Elghobashi, S. E. "An updated classification map of particle-laden turbulent flows ", **Proceedings of IUTAM Symposium on Computational approaches to multiphase flow** , Springer pp. 3-10, , (2006).

B5 Loy, A.C., Jing, J., Zhang, J., Wang., Y., Elghobashi, S., Chen, Z. and Wong, B.J.F. "Anatomic optical coherence tomography of upper airways", **Optical Coherence Tomography: Technology and Applications,** Ed. W. Drexler and J. Fujimoto, Springer, Chapter 75, pp. 1145-2262, (2015).

Guest Editor

Elghobashi, S.E. " Point-Particle Models for Disperse Turbulent Flows", **International Journal of Multiphase Flow, Special Issue**, Volume 35, Issue 9, Pages 791-878, (September 2009).

Journal Papers

J1 Elghobashi, S.E., Pun, W.M. and Spalding, D.B., "Concentration Fluctuations in Isothermal Turbulent Confined Coaxial Jets",
Chem. Eng. Sci., Vol. 32, pp. 161-166 (1977).

J2 Elghobashi, S.E. and Wassel, A.T., "The Effect of Turbulent Heat Transfer on the Propagation of an Optical Beam Across Supersonic Boundary and Free Shear Layers",
Int. J. Heat and Mass Transfer, Vol. 23,pp.1229-1241 (1980).

J3 Elghobashi, S.E., Samuelsen, G.S., Wuerer, J.E., and LaRue, J.C., " Prediction and Measurement of Mass, Heat and Momentum Transport in a Nonreacting Turbulent Flow of a Jet in an Opposing Stream",
J. Fluids Engineering, Vol. 103, pp. 127-132 (1981).

J4 Megahed, I.E.A. and Elghobashi, S.E., "On the Numerical Solution of Indeterminate Steady Elliptic Flows",
Computer Methods in Applied Mechanics and Engineering, Vol. 26, pp. 225-240 (1981).

J5 Elghobashi, S.E. and Megahed, I.E.A., "Mass and Momentum Transport in a Laminar Isothermal Two-Phase Round Jet",
Int. J. Numerical Heat Transfer, Vol. 4 , pp. 317-329 (1981).

J6 Elghobashi, S.E. and Abou Arab, T.W., "A Two-Equation Turbulence Model for Two-Phase Flows",
Physics of Fluids, Vol. 26 , pp.931-938 (1983).

J7 Elghobashi, S.E. and Launder, B.E., "Turbulent Time Scales and the Dissipation Rate of Temperature Variance in the Thermal Mixing",
Physics of Fluids, Vol. 26 ,pp. 2415-2419 (1983).

J8 Modarress, D., Tan, H. and Elghobashi, S.E., "Two-Component LDA Measurement in a Two-Phase Turbulent Jet",
AIAA J. Vol. 22, pp. 624-630 (1984).

J9 Modarress, D., Wuerer, J. and Elghobashi, S.E., "An Experimental Study of a Turbulent Round Two-Phase Jet",
Chemical Engineering Communications, Vol. 28, pp. 341-354 (1984).

J10 Wassel, A.T. and Elghobashi, S.E., "Mathematical Simulation of Ocean Thermal Energy Conversion Sea Water Systems",
J. Solar Energy Engineering Vol. 106, pp. 198-205 (1984).

J11 Mostafa A.A. and Elghobashi, S.E., "A Study of the Motion of Vaporizing Droplets in a Turbulent Flow",
AIAA Progress in Astronautics and Aeronautics, Vol. 10,pp. 513-539 ,Oppenhiem and Soloukhin (editors) (1984).

J12 Elghobashi, S.E., Abou-Arab, T., Rizk, M. and Mostafa, A., "Prediction of the Particle-Laden Jet with a Two-Equation Turbulence Model",
Int. J. of Multiphase Flow, Vol. 10, pp. 697-710 (1984).

J13 Bellan J., and Elghobashi, S.E., "Fuel Composition Effects on High Temperature Corrosion in Boiler and Furnaces",
J. of Engineering for Power, Vol. 107, pp. 744-757 (1985).

J14 Rizk, M., and Elghobashi, S.E., "Wall Effects on the Motion of a Spherical Particle Suspended in a Turbulent Flow",
Physics of Fluids, Vol. 28, pp. 806-817 (1985).

J15 Mostafa, A.A. and Elghobashi, S.E., "A Two-Equation Turbulence Model for Jet Flows Laden with Vaporizing Droplets",
Int. J. of Multiphase Flow, Vol. 11, pp. 515-533 (1985).

J16 Schumann, U., Elghobashi, S.E., and Gerz, T., "Direct Simulation of Stably Stratified Turbulent Homogeneous Shear Flows",
Notes on Numerical Fluid Mechanics, Vol. 15, pp. 245-264 (1986).

J17 Prud'homme, M., and Elghobashi, S.E., "Turbulent Heat Transfer Near the Reattachment of Flow Downstream of a Sudden Pipe Expansion",
Int. J. Numerical Heat Transfer, Vol. 10, pp. 349-368 (1986).

J18 Conner, J. and Elghobashi, S.E., "Numerical Solution of Laminar Flow Past a Sphere with Surface Mass Transfer",
Int. J. Numerical Heat Transfer, Vol. 12, pp. 57-82 (1987).

J19 Rizk, M. and Elghobashi, S.E., "A Two-Equation Turbulence Model for Dispersed Dilute Two-Phase Confined Flows",
Int. J. of Multiphase Flow, Vol. 15, pp. 119-133 (1989).

J20 Gerz, T., Schumann, U. and Elghobashi, S., "Direct Simulation of Stably Stratified Homogeneous Turbulent Shear Flows",
J. Fluid Mechanics, Vol. 200, pp. 563-594 (1989).

J21 Tsau, F. , Elghobashi, S. E.,and Sirignano, W. " Effects of G- Jitter on a Thermally Buoyant Flow",
J. Thermophysics and Heat Transfer, vol. 6, pp. 246-254 (1992).

J22 Elghobashi, S. E., "Particle-Laden Turbulent Flows : Direct Simulation and Closure Models ",
J. Applied Scientific Research, vol.48, pp. 301-314 (1991).

J23 Elghobashi, S. E.,and Truesdell, G.C., "Direct Simulation of Particle Dispersion in a Decaying Isotropic Turbulence",
J. Fluid Mechanics, vol. 242, pp. 655-700 (1992).

J24 Nomura, K.N.,and Elghobashi, S. E. "Mixing characteristics of an inhomoge-

neous scalar in isotropic and homogeneous sheared turbulence",
Physics of Fluids, vol. 4, pp. 606-625 (1992).

J25 Kim, I. , Elghobashi, S. E., and Sirignano, W. " Three- dimensional flow over two spheres placed side by side",
J. Fluid Mechanics, vol. 246, pp. 465-488 (1993).

J26 Nomura, K.N.,and Elghobashi, S. E. " The structure of inhomogeneous turbulence in variable density nonpremixed flames",
Theoretical and Computational Fluid Dynamics, vol. 5, pp. 153-176 (1993).

J27 Elghobashi, S. E., and Truesdell, G.C., " On the two-way interaction between homogeneous turbulence and dispersed solid particles ; Part 1 : turbulence modification",
Physics of Fluids, vol. A5, pp. 1790-1801 (1993).

J28 Elghobashi, S. E., 'On Predicting Particle-Laden Turbulent Flows' ,
J. Applied Scientific Research, Vol. 52, 4, pp. 309-329 (1994).

J29 Truesdell, G.C., and Elghobashi, S. E." On the two-way interaction between homogeneous turbulence and dispersed solid particles ; Part 2 : particle dispersion",
Physics of Fluids, Vol. 6, pp. 1405-1407 (1994).

J30 Kim, I. , Elghobashi, S. E., and Sirignano, W. " Unsteady flow interactions between an advected cylindrical vortex tube and a spherical particle",
J. Fluid Mechanics, Vol. 288, pp. 123-155 (1995).

J31 Boratav, O. , Elghobashi, S. E., and Zhong, R. " On the alignment of the α—strain and vorticity in turbulent nonpremixed flames",
Physics of Fluids, Vol. 8, pp. 2251-2253 (1996).

J32 Kim, I. , Elghobashi, S. E., and Sirignano, W. " Unsteady flow interactions between a pair of advected vortex tubes and a rigid sphere",
International J. Multiphase Flow, Vol. 23, pp. 1-23 (1997).

J33 Druzhinin, O. and Elghobashi, S., ' DNS of bubble-laden turbulent flows using the two-fluid formulation',
Physics of Fluids, Vol. 10, pp. 685-697 (1998).

J34 Kim, I. , Elghobashi, S. E., and Sirignano, W. ' On the equation for spherical particle motion : effects of Reynolds and acceleration numbers',
J. Fluid Mechanics, Vol. 367, pp. 221-253 (1998).

J35 Boratav, O. , Elghobashi, S. E., and Zhong, R.' On the alignment of strain,

vorticity and scalar gradient in turbulent, buoyant, nonpremixed flames',
Physics of Fluids, Vol. 10, pp. 2260-2267 (1998).

J36 Druzhinin, O. and Elghobashi, S., 'On the decay rate of isotropic turbulence laden with microparticles',
Physics of Fluids, Vol. 11, pp. 602-610 (1999).

J37 Druzhinin, O. and Elghobashi, S., ' A Lagrangian-Eulerian mapping solver for direct numerical simulation of a bubble-laden homogeneous turbulent shear flow using the two-fluid formulation ',
J. Computational Physics, Vol. 154, pp.174-196 (1999).

J38 Elghobashi, S. E., Zhong, R. and Boratav, O. ' Effects of gravity on turbulent nonpremixed flames',
Physics of Fluids, Vol. 11 , pp. 3123-3135 (1999).

J39 Zhong, R. , Elghobashi, S. E., Boratav, O. ' Surface topology of a buoyant turbulent nonpremixed flame',
Physics of Fluids, Vol. 12, pp. 2091-2100 (2000).

J40 Ahmed, A.M. and Elghobashi, S. E. On the mechanisms of modifying the structure of turbulent homogeneous shear flows by dispersed particles,
Physics of Fluids, Vol. 12, pp. 2906-2930 (2000).

J41 Druzhinin, O. and Elghobashi, S., ' Direct numerical simulation of a three-dimensional spatially-developing bubble-laden mixing layer with two-way coupling',
J. Fluid Mechanics, Vol. 429, pp. 23-61 (2001).

J42 Ahmed, A.M. and Elghobashi, S. E. Direct numerical simulation of particle dispersion in homogeneous turbulent shear flows ,
Physics of Fluids, Vol. 13, pp. 3346-3364 (2001).

J43 Ferrante, A. and Elghobashi, S. E. On the physical mechanisms of two-way coupling in particle-laden isotropic turbulence ,
Physics of Fluids, Vol. 15, pp. 315-329 (2003).

J44 Ferrante, A. and Elghobashi, S. E., ' A robust method for generating inflow conditions for direct simulations of spatially-developing turbulent boundary layers',
J. Computational Physics, Vol. 198, pp. 372-387 (2004).

J45 Latz, M. I., Juhl, A. R., Ahmed, A.M., Elghobashi, S. and Rohr, J. ' Hydrodynamic stimulation of dinoflagellate bioluminescence: A computational and experimental study',
J. Experimental Biology, Vol. 207, pp. 1941-1951(2004).

J46 Ferrante, A. and Elghobashi, S. E., ' On the physical mechanisms of drag reduction in a spatially-developing turbulent boundary layer laden with microbubbles', **J. Fluid Mechanics**, Vol. 503, pp. 345-355. (2004).

J47 Ferrante, A. and Elghobashi, S. E., Adams P., Valenciano M. and Longmire D. ' Evolution of quasi-streamwise vortex tubes and wall-streaks in a microbubble-laden turbulent boundary layer over a flat plate',
Physics of Fluids, Vol. 16(9), pp. S2 (2004).

J48 Ferrante, A. and Elghobashi, S. E., ' Reynolds number effect on drag reduction in a microbubble-laden spatially-developing turbulent boundary layer',
J. Fluid Mechanics, Vol. 543, pp. 93-106 (2005).

J49 Ferrante, A. and Elghobashi, S. E., ' On the effects of microbubbles on the Taylor-Green vortex flow',
J. Fluid Mechanics, Vol. 572 , pp. 145 - 177 (2007).

J50 Ferrante, A. and Elghobashi, S. E., ' On the accuracy of the two-fluid formulation in DNS of bubble-laden turbulent boundary layers',
Physics of Fluids, Vol. 19, 045105, pp.1-8 (2007).

J51 L'vov, V.S., Pomyalov, A., Ferrante, A. and Elghobashi, S. E., ' Analytical model of the time Developing turbulent boundary layer',
J. Exp. Theor. Phys., Vol. 86, issue 2, pp. 111-116 (2007).

J52 Lucci, F., Ferrante, A. and Elghobashi, S. E., ' Modulation of isotropic turbulence by particles of Taylor-lengthscale size',
J. Fluid Mechanics, Vol. 650, pp. 5-55 (2010).

J53 Lucci, F., Ferrante, A. and Elghobashi, S. ' Is Stokes number an appropriate indicator of turbulence modulation by large particles ?'
Physics of Fluids, Vol. 23, pp. 25101-1-7 (2011).

J54 Cleckler, J., Elghobashi, S. and Liu, F. 'On the motion of inertial particles by sound waves'
Physics of Fluids, Vol. 24, 033301 (2012).

J55 Lucci, F., L'Vov, V., Ferrante, A., Rosso, M. and Elghobashi, S. , ' Eulerian-Lagrangian bridge for the energy and dissipation spectra in isotropic turbulence ',
Theoretical and Computational Fluid Dynamics, DOI: 10.1007/s00162-013-0310-5(2013).

J56 Wang, Y. and Elghobashi, S. , ' On locating the obstruction in the upper

airway via numerical simulation ',
J. Respiratory Physiology & Neurobiology, Vol. 193, pp.1-10 (2014).

J57 Mylavarapu, G., Wang, Y., Elghobashi, S. and Gutmark, E. 'PIV measurements and numerical simulations of the flow in a human upper airway phantom', **Biomechanics and Modeling in Mechanobiology**, submitted (2016).

Archival Conference Papers

C1 Elghobashi, S.E. and Pun, W.M., "A Theoretical and Experimental Study of Turbulent Diffusion Flames in Cylindrical Furnaces", **Proceedings of Fifteenth Symposium (International) on Combustion**, (1974).

C2 Elghobashi, S.E., Pratt, D.T., Spalding, D.B. and Srivatsa, S.K., "Unsteady Combustion of Fuel Spray in Jet Engine Afterburners", **Proceedings of Third International Symposium on Air Breathing Engines**, Munich (1976).

C3 Elghobashi, S.E. and Launder, B.E., "Modeling the Dissipation Rate of Scalar Fluctuations in a Thermal Mixing Layer", **Proceedings of Third Symposium on Turbulent Shear Flows**, (1981).

C4 Elghobashi, S.E. and Abou Arab, T.W., "A Second Order Turbulence Model for Two-Phase Flows", **Proceedings of Seventh International Heat Transfer Conference**, Munich (1982).

C5 Elghobashi, S.E. and Prud'homme, M., "On the Accuracy and Stability of Quadratic Upstream Differencing in Laminar Elliptic Flows", **Numerical Methods in Laminar and Turbulent Flow**, ed. Taylor, C., Johnson, J., and Smith, W., Pineridge Press, U.K., pp. 317-327 (1983).

C6 Mostafa A.A. and Elghobashi, S.E., "A Study of the Motion of Vaporizing Droplets in a Turbulent Flow", **Proceedings of Ninth International Colloquium and Dynamics of Explosions and Reactive Systems**, Poitiers, France, July (1983).

C7 Elghobashi, S.E., Abou Arab, T.W., Rizk, M. and Mostafa, A., "A Mathematical Model of the Turbulent Two-Phase Round Jet",**Proceedings of Fourth International Symposium on Turbulent Shear Flows**, Karlsruhe,
Germany, Sept. (1983).

C8 Elghobashi, S.E., Rizk, M. and Mostafa, A., "A Mathematical Model of the Two- Phase Turbulent Axisymmetric Jet" , **Proceedings of the Third Multi-Phase Flow and Heat Transfer Symposium**, Miami, Florida, April (1983).

C9 Prud'homme, M. and Elghobashi, S.E., "Prediction of Wall-Bounded Turbulent Flows with an Improved Version of a Reynolds-Stress Model",
Proceedings of Fourth International Symposium on Turbulent Shear Flows, Karlsruhe, Germany, Sept. (1983).

C10 Elghobashi, S.E. and J.C. LaRue, "The Effect of Mechanical Strain on the Dissipation Rate of a Scalar Variance", **Proceedings of Fourth International Sym-**

posium on Turbulent Shear Flows, Karlsruhe, Germany, Sept. (1983).

C11 Rizk, M. and Elghobashi, S.E., "A Mathematical Model for a Turbulent Gas-Solid Suspension Flow in a Vertical Pipe", **Proceedings of Fifth International Symposium on Turbulent Shear Flows**, Cornell Univ., August (1985).

C12 Elghobashi, S.E., Gerz, T. and Schumann, U., "Direct Simulation of Turbulent Homogeneous Shear Flow with Buoyancy", **Proceedings of Fifth International Symposium on Turbulent Shear Flows**, Cornell Univ., August (1985).

C13 Elghobashi, S.E., Gerz, T. and Schumann, U., "Direct Simulation of the Initial Development and the Homogeneous Limit of the Thermal Mixing Layer", **Proceedings of Sixth International Symposium on Turbulent Shear Flows**, Toulouse, France, (1987).

C14 Elghobashi, S. E.,and Nomura, K.N., "Direct Simulation of a Fast Chemical Reaction in a Homogeneous Turbulent Shear Flow", **Proceedings of Seventh Symposium on Turbulent Shear Flows**, Stanford, pp. 711-716 (1989).

C15 Elghobashi, S. E., and Truesdell, G.C., "Direct Simulation of Particle Dispersion in a Decaying Grid Turbulence", **Proceedings of Seventh Symposium on Turbulent Shear Flows**, Poster Session, Stanford (1989).

C16 Tsau, F. , Elghobashi, S. E., and Sirignano, W. " Effects of G- Jitter on a Thermal Buoyant Flow", Paper no 90-653, **AIAA 28th Aerospace Science Meeting**, Reno, Nevada, January (1990).

C17 Tsau, F. , Elghobashi, S. E.,and Sirignano, W. " Prediction of a Liquid Jet in a Gaseous Crossflow", Paper no 90-2067, **AIAA 26th Joint Propulsion Conference**, Orlando, Florida, July (1990).

C18 Nomura, K.N., and Elghobashi, S. E. "Direct Simulation of an Isothermal Nonpremixed Flame in a Homogeneous Turbulent Shear Flow", Paper no 90-148, **AIAA 28th Aerospace Science Meeting**, Reno, Nevada, January (1990).

C19 Kim, I. , Elghobashi, S. E., and Sirignano, W. " Three- dimensional droplet interactions in dense sprays", Paper no 91-0073, **AIAA 30th Aerospace Science Meeting**, Reno, Nevada, January (1991).

C20 Truesdell, G.C., and Elghobashi, S. E. "Direct numerical simulation of a particle-laden homogeneous turbulent flow ", **Proceedings of First ASME-JSME Fluids Engineering Conference**, Portland, Oregon, ASME-FED, Vol. 121, pp. 11-17, June

(1991).

C21 Elghobashi, S. E., and Truesdell, G.C., "On the interaction between solid particles and decaying turbulence ", **Proceedings of Eighth Symposium on Turbulent Shear Flows**, Munich, Germany , September (1991).

C22 Sirignano, W.A., Chiang, C.H., Kim, I. and Elghobashi, S. E. " Aerodynamic interactions amongst neighboring droplets", **4th International Symposium on Computational Fluid Dynamics**, Davis, Calif., September (1991).

C23 Kim, I. , Elghobashi, S. E., and Sirignano, W. " Three- dimensional flow computation for two interacting, moving droplets", Paper no 92-0343, **AIAA 30th Aerospace Science Meeting**, Reno, Nevada, January (1992).

C24 Nomura, K.N., and Elghobashi, S. E. " The structure of inhomogeneous turbulence in variable density nonpremixed flames", **Proceedings of IUTAM Symposium on Eddy Structure and Identification in Free Turbulent Shear Flows**, Poitiers, France, October (1992).

C25 Elghobashi, S. E. and Truesdell, G.C., " On the two-way interaction between homogeneous turbulence and dispersed solid particles", Papaer AIAA 93-1875, **AIAA /ASME 29th Joint Propulsion Conference**, Monterey, CA (1993).

C26 Elghobashi, S. E." On Predicting particle-laden turbulent flows ", **Proceedings of Seventh Workshop on Two-Phase Flows, Erlangen**, Germany, pp 211-219, April 11 (1994). [**Invited Lecture**]

C27 Elghobashi, S. E." Effects of the two-way coupling on particle dispersion ", **Proceedings of Seventh Workshop on Two-Phase Flows, Erlangen, Germany**, pp 224-230, April 13 (1994). [**Invited Lecture**]

C28 Kim, I. , Elghobashi, S. E., and Sirignano, W. " Unsteady flow interactions between a pair of advected cylindrical vortex tube and a rigid sphere", Paper no 95-0105, **AIAA 33th Aerospace Science Meeting**, Reno, Nevada, January (1995).

C29 Elghobashi, S. E., Lee, Y.Y. and Zhong, R. " Effects of gravity on sheared and nonsheared turbulent nonpremixed flame", **Third International Microgravity Combustion Workshop, NASA Lewis"**, Cleveland, Ohio, April 11-13 (1995).

C30 Kim, I. , Elghobashi, S. E., and Sirignano, W. " " The motion of a spherical particle in unsteady flows at moderate Reynolds numbers", **AIAA, 34th Aerospace Sciences Meeting**, Reno, NV, January (1996).

C31 Elghobashi, S. "Direct simulation of dispersed dilute two-phase turbulent flows",

Part 1: Decaying Turbulence, **Proceedings of the 1996 Lecture series programme, Von Karman Institute for Fluid Dynamics**, Rhode-Saint-Genese, Belgium, January 29-February 2, 1996. [**Invited Lecture**]

C32 Elghobashi, S. "Direct simulation of dispersed dilute two-phase turbulent flows", Part 2 : Homogeneous shear, **Proceedings of the 1996 Lecture series programme, Von Karman Institute for Fluid Dynamics**, Rhode-Saint-Genese, Belgium, January 29-February 2, 1996. [**Invited Lecture**]

C33 Elghobashi, S. and Lasheras, J. " Effects of gravity on sheared turbulence laden with bubbles or droplets", **Third Microgravity Fluid Physics Conference, NASA Lewis**, Cleveland, OH, June 13-15, 1996.

C34 Elghobashi, S., Boratav, O. and Zhong, R. " Effects of gravity on sheared and nonsheared turbulent nonpremixed flames", **Fourth International Microgravity Combustion Conference, NASA Lewis**, Cleveland, OH, May 19-21, 1997.

C35 Elghobashi, S. and Ahmed, A.M. ' DNS of turbulent homogeneous shear flow laden with particles: Two-way coupling', **Japan Society of Mechanical Engineers, Centennial Grand Congress,** Tokyo, Japan, July 18-19, 1997. [**Invited Lecture**]

C36 Druzhinin, O. and Elghobashi, S. 'DNS of bubble-laden turbulent flows using a two-fluid formulation', **Third International Conference on Multiphase Flow,** Lyon, France, June 8-12, 1998.

C37 Elghobashi, S. and Lasheras, J. 'Effects of gravity on sheared turbulence laden with bubbles or droplets' **Fourth Microgravity Fluid Physics and Transport Phenomena Conference,** NASA-Lewis, Cleveland, Ohio, August 12-14, 1998.

C38 Elghobashi, S. and Zhong, R. 'Effects of gravity on sheared turbulent nonpremixed flames' **Fifth International Microgravity Combustion Conference,** NASA-Lewis, Cleveland, Ohio, May 18-20, 1999.

C39 Elghobashi, S. " On the two-fluid and trajectory approaches for DNS of turbulent particle-laden flows", Part 1: DNS of bubble-laden flows via the two-fluid approach, **Proceedings of the 2000 Lecture series programme, Von Karman Institute for Fluid Dynamics**, Rhode-Saint-Genese, Belgium, April 3-7, 2000. [**Invited Lecture**]

C40 Elghobashi, S. " On the two-fluid and trajectory approaches for DNS of turbulent particle-laden flows", Part 2: On the approximation of the two-way coupling terms in the trajectory approach, **Proceedings of the 2000 Lecture series programme, Von Karman Institute for Fluid Dynamics**, Rhode-Saint-Genese, Belgium, April 3-7, 2000. [**Invited Lecture**]

C41 Ferrante, A. and Elghobashi, S. 'Effects of Reynolds number on drag reduction in a microbubble-laden spatially-developing turbulent boundary layer' **Second International Symposium on Seawater Drag Reduction,** Busan, Korea, May 23-26, 2005.

C42 Ferrante, A. and Elghobashi, S. ' On the accuracy of the two-fluid formulation in DNS of a microbubble-laden turbulent boundary layer 26^{th} **Symposium on Naval Hydrodynamics,** Rome, Italy, 17-22 September 2006.

C43 Ferrante, A. and Elghobashi, S. ' On the effects of finite-size particles on decaying isotropic turbulence' **International Conference on Multiphase Flow, ICMF 2007,** Leipzig, Germany, July 9 – 13, 2007.

C44 Lucci, F., Ferrante, A. and Elghobashi, S. ' Turbulence modulation by particles of the Taylor-lengthscale size: is Stokes number an appropriate indicator ?' **International Conference on Multiphase Flow, ICMF 2010,** Tampa, Florida, May 30- June 4, 2010.

Abstracts of Papers Presented at Conferences

A1 Mostafa A.A. and Elghobashi, S.E., "Prediction of a Turbulent Round Gaseous Jet Laden with Vaporizing Droplets", Western States/The Combustion Institute, UCLA, October (1983).

A2 Bellan J. and Elghobashi, S.E., "Impact of Fuel Composition on Deposits and on High-Temperature Corrosion in Industrial Furnaces", Western States Meeting, The Combustion Institute, UCLA, October (1983).

A3 Rizk, M. and Elghobashi, S.E., "Turbulent Fluid and Particle Interaction Near a Plane Wall", **Bull. Am. Phys. Soc.**, Vol. 28, pp. 1378 (1983).

A4 Rizk, M. and Elghobashi, S.E., "The Motion of a Spherical Particle Suspended in a Turbulent Flow Near a Plane Wall", **Proceedings of International Symposium on Two-Phase Annular and Dispersed Flows**, Pisa, Italy, June (1984).

A5 Elghobashi, S. E., and Truesdell, G.C., "Direct Simulation of Particle Dispersion in a Homogeneous Turbulent Shear Flow", Paper no. 73 f ,**AIChE Annual Meeting**, San Francisco, November (1989).

A6 Elghobashi, S. E. "Direct numerical simulation and modelling of particle-laden turbulent flows", **Shell Conference on Computational Fluid Dynamics** , Apeldoorn, The Netherlands, December 11,1989.

A7 Elghobashi, S. E., and Truesdell, G.C., "Direct Simulation of Particle Dispersion in Grid Turbulence and Homogeneous Shear Flows", **Bull. Am. Phys. Soc.**, Vol. 34, pp. 2311 (1989).

A8 Elghobashi, S. E., and Truesdell, G.C., "Direct Numerical Simulation of Particle-Laden Decaying Isotropic Turbulence", **21st Annual Meeting of The Fine Particle Society**, San Diego, Calif., August (1990).

A9 Kim, I. , Elghobashi, S. E., and Sirignano, W. " Three- dimensional flow interactions between two neighboring spheres", **Bull. Am. Phys. Soc.**, Vol. 36, pp. 2622 (1991).

A10 Elghobashi, S. E., and Truesdell, G.C., " On the modification of the energy spectrum of homogeneous turbulence by dispersed solid particles ", **Proceedings of Sixth Workshop on Two-Phase Flows**, Erlangen, Germany, pp 211-219, March 30 (1992). [**Invited Lecture**]

A11 Elghobashi, S. E., " On predicting particle-laden turbulent flows", **Workshop**

on turbulence in particulate multiphase flow, Fluid Dynamics Laboratory, Battelle Pacific Northwest Laboratory, Richland, WA, March 22, 1993.[**Invited Lecture**]

A12 Elghobashi, S. E., " Direct numerical simulation of particle dispersion and turbulence modulation in homogeneous turbulence", **NATO Advanced Research Workshop on Chaotic Advection, Tracer Dynamics, and Turbulent Dispersion**, Alessandria, Italy, May 24-28, 1993. [**Invited Lecture**]

A13
Elghobashi, S. E." One of the unresolved questions in predicting particle-laden turbulent flows ", **International Symposium on Numerical Methods for Multiphase Flows**, Lake Tahoe, NV, June 19-24 (1994). [**Invited Lecture**]

A14 Elghobashi, S. E." Mathematical models of particle-laden turbulent flows ", **Proceedings of 2nd International Workshop on Mathematical Modeling of Turbulent Flows, Tokyo**, Japan, July 29 (1994). [**Invited Lecture**]

A15 Elghobashi, S. E." Direct numerical simulation of particle-laden homogeneous turbulence ", **Proceedings of of 2nd International Workshop on Mathematical Modeling of Turbulent Flows, Tokyo**, Japan, July 30 (1994). [**Invited Lecture**]

A16 Nomura, K.N., and Elghobashi, S. E. "Interaction of chemical energy release and small-scale turbulence in a nonpremixed reacting flow", **47th Annual Meating of the American Physical Society**, Div. of Fluid Dynamics, Atlanta, GA, (1994).

A17 Elghobashi, S. E." DNS of bubble dispersion in homogeneous turbulent shear flows ", **ONR bubbly flow workshop**, UC San Diego, February 23-24 (1995).

A18 Elghobashi, S. E. "Direct simulation of particle dispersion in a homogeneous turbulent shear flow", Presented at the **Annual ASME/JSME Fluids Engineering Conference**, Hilton Head, S.C., August 13-18, (1995). **[Invited lecture]**

A19 Elghobashi, S., Boratav, O. and Zhong, R. 'Buoyancy effects on the structure of turbulence in nonpremixed flames', **48th Annual Meeting of American Physical Society**, Div. Fluid Dynamics, Irvine, CA, November 1995.

A20 Elghobashi, S. and Ahmed, A. " Bubble dispersion and turbulence modification in a homogeneous shear flow", **ONR workshop on Bubbly Flows**, UCSD, La Jolla, February 22-23, 1996.

A21 Elghobashi, S., Boratav, O. and Zhong, R. "Effects of buoyancy on turbulent nonpremixed flames', Presented at the **'International Conference on Turbulent Heat Transfer'**, San Diego, CA, March 10-15, 1996. **[Invited lecture]**

A22 Boratav, O. Elghobashi, S. and Zhong, R. 'Buoyancy effects on the struc-

ture of turbulence in nonpremixed flames', **SIAM - 6th International Conference on Numerical Combustion,** New Orleans, March 4-6, 1996.

A23 Elghobashi, S. and Ahmed, A. "On the two-way interactions between a turbulent homogeneous shear flow and dispersed particles", **Eighth Workshop on Turbulent Two-Phase Flows**, Merseburg, Germany, March 25-29, 1996.**[Invited lecture]**

A24 Elghobashi, S. " How do particles modify the turbulence energy of homogeneous shear flows ?", **ASME Fluids Engineering Conference**, San Diego, CA, July 8-11, 1996. **[Invited Lecture]**

A25 Elghobashi, S. and Ahmed, A. " How do particles modify the turbulence energy of homogeneous shear flows ?", **49th Annual Meeting of American Physical Society,** Div. Fluid Dynamics, Syracuse, NY, November 1996.

A26 Elghobashi, S., Zhong, R. and Boratav, O. " Evolution of flame surface in buoyant and nonbuoyant turbulent nonpremixed reactions", **49th Annual Meeting of American Physical Society,** Div. Fluid Dynamics, Syracuse, NY, November 1996.

A27 Latz, M., Juhl, A., Elghobashi, S., Ahmed, A. and Rohr, J. "Response of dinoflagellates in well-characterized laminar and turbulent flows: differentiating the effect of shear and acceleration", **Annual meeting of the American Society of Limnology and Oceanography (ASLO)**, Santa Fe, New Mexico, February 1997.

A28 Druzhinin, O. and Elghobashi, S. " A closure model for bubble-laden turbulent flows" **ONR workshop on Dynamics of Bubbly Flows, UCSD, February 19-21, 1997.**

A29 Elghobashi, S. " Modification of a homogeneous turbulent shear flow by dispersed particles" **Workshop on Turbulence Transport and Numerical Modeling, Center for Nonlinear Studies,** Los Alamos National Laboratory, June 3-7, 1997.**[Invited Lecture]**

A30 Elghobashi, S. and Druzhinin, O. " DNS of bubble-laden turbulent flows using the two-fluid formulation" **50th Annual Meeting of American Physical Society,** Div. Fluid Dynamics, San Francisco, CA, November 1997.

A31 Boratav, O., Elghobashi, S. and Zhong, R. " Persistence of strain in buoyant and nonbuoyant turbulent nonpremixed flames" **50th Annual Meeting of American Physical Society,** Div. Fluid Dynamics, San Francisco, CA, November 1997.

A32 Elghobashi, S. and Druzhinin, O. " DNS of bubble-laden turbulent flows using the two-fluid formulation" **ONR workshop on Dynamics of Bubbly Flows,** Caltech, February 25-27, 1998.

A33 Druzhinin, O. and Elghobashi, S. " A Lagrangian-Eulerian mapping solver for DNS of a bubble-laden homogeneous turbulent shear flow using the two-fluid formulation" **51st Annual Meeting of American Physical Society, Div. Fluid Dynamics,Philadelphia, PA,** November 22-24, 1998. Published in **Bulletin of APS, Vo. 43, 1965-2144, 1998.**

A34 Druzhinin, O. and Elghobashi, S. " A bubble-laden turbulent mixing layer: DNS and Closure model" **ONR workshop on Dynamics of Bubbly Flows,** UCSD, February 24-26, 1999.

A35 Druzhinin, O. and Elghobashi, S. " On the point-force approximation in DNS of particle-laden flows with two-way coupling " **51st Annual Meeting of American Physical Society, Div. Fluid Dynamics,New Orleans,LA** November 21-23, 1999. Published in **Bulletin of APS, Vol. 44, 15-194, 1999**

A36 Druzhinin, O. and Elghobashi, S. " DNS and Closure model for a bubble-laden turbulent mixing layer:" **ONR workshop on Dynamics of Bubbly Flows,** CALTECH, March 1-3, 2000. *

A37 Druzhinin, O. and Elghobashi, S. " On the point-force approximation in DNS of prticle-laden turbulent flows with two-way coupling", ERCOFTAC Conference on Dynamics of Particle-Laden Flows, Zurich, Switzerland, July 3-5, 2000.

A38 Elghobashi, S. " Recent Advance in DNS of Particle-Laden Turbulent Flows" **[Invited Plenary lecture], XI Congres on Numerical Methods and their Applications, ENIEF 2000** ,San Carlos de Bariloche, Argentina, November 2000.

A39 Druzhinin, O. and Elghobashi, S. " The properties of a spatially-developing bubble-laden mixing layer with two-way coupling" **53rd Annual Meeting of American Physical Society,** Div. Fluid Dynamics, Washington D.C., November 2000.

A40 Ahmed, A. and Elghobashi, S. " On the physical mechanisms of modifying the structure of turbulent homogeneous shear flows by dispersed particles " **53rd Annual Meeting of American Physical Society,** Div. Fluid Dynamics, Washington D.C., November 2000.

A41 Elghobashi, S. E." DNS of bubble-laden turbulent shear flows ", **ONR bubbly flow workshop,** CALTECH, Pasadena, April 17-19, 2001.

A42 Druzhinin, O. and Elghobashi, S. 'Direct numerical simulation of a three-dimensional spatially-developing bubble-laden mixing layer with two-way coupling', **4th International Conference on Multiphase Flow-ICMF 2001,** New Orleans, May 26-31, 2001.

A43 Elghobashi, S." The physical mechanisms of modifying the structure of turbulent homogeneous shear flows by dispersed particles ", **Euromech Colloqium 421: Strongly-Coupled Dispersed Two-Phase Flows** , LEGI, Grenoble, France, September 10-12, 2001.

A44 Elghobashi, S." The physical mechanisms of modifying the structure of turbulent homogeneous flows by dispersed particles ", **[Invited Plenary Lecture], ER-COFTAC Conference on Small Particles in Turbulence** , Seville, Spain, March 11-13, 2002.

A45 Elghobashi, S. and Ferrante, A. " DNS of bubble-laden spatially-developing turbulent boundary layer with one-way coupling" **ONR workshop on Dynamics of Bubbly Flows,** UCSD, La Jolla, Calif., April 3-4, 2002.

A46 Ferrante, A. and Elghobashi, S. " Dispersion of bubbles in a spatially-developing turbulent boundary layer" **55th Annual Meeting of American Physical Society,** Div. Fluid Dynamics, Dallas, Texas, November 2002.

A47 Elghobashi, S. and Ferrante, A. " DNS of bubble-laden spatially-developing turbulent boundary layer with two-way coupling" **ONR workshop on Waves and Dynamics of Bubbly Flows,** Caltech, Pasadena, Calif.,February 19-20, 2003.

A48 Elghobashi, S. and Ferrante, A. " DNS of bubble-laden spatially-developing turbulent boundary layer" **5th Euromech Fluid Mechanics Conference,** Toulouse, France, August 24-28, 2003.

A49 Ferrante, A. and Elghobashi, S. "Drag reduction in a spatially-developing turbulent boundary layer laden with microbubbles," **ERCOFTAC Multiphase Flow Conference, ETH, Zurich, Switzerland,** November, 2003.

A50 Elghobashi, S. and Ferrante, A. " Drag reduction in a bubble-laden spatially-developing turbulent boundary layer over a flat plate", **56th Annual Meeting of American Physical Society,** Div. Fluid Dynamics, East Rutherford, New Jersey, November 2003. Published in **Bulletin of APS, Vol. 48, p.116, 2003.**

A51 Ferrante, A. and Elghobashi, S. " A method for generating inflow conditions for direct simulations of spatially-developing turbulent boundary layers" **56th Annual Meeting of American Physical Society,** Div. Fluid Dynamics, East Rutherford, New Jersey, November 2003. Published in **Bulletin of APS, Vol. 48, p.119, 2003.**

A52 Elghobashi, S. and Ferrante, A. " The physical mechanisms of drag reduction in a microbubble-laden turbulent boundary layer with one-way coupling" **ONR workshop on Dynamics of Bubbly Flows,** UCSD, La Jolla, Calif., March 24-25, 2004.

A53 Elghobashi, S. "On the physical mechanisms of drag reduction in a mirobubble-laden turbulent boundary layer" **Keynote Lecture at The 5th International Conference of Multiphase Flow (ICMF 2004)**, Yokohama, Japan, May 31 - June 3, 2004.

A54 Elghobashi, S. " On the drag reduction in a mirobubble-laden spatially-developing turbulent boundary layer", IUTAM Symposium on Recent advances in disperse multiphase flow simulation- **[Invited Lecture]**- Chicago-October 2004.

A55 Ferrante, A. and Elghobashi, S. " Effects of bubble diameter on drag reduction in a spatially developing turbulent boundary layer over a flat plate", **57th Annual Meeting of American Physical Society,** Div. Fluid Dynamics, Seattle, Washington, November 2004. Published in **Bulletin of APS, Vol. 49, p.129, 2004.**

A56 Elghobashi, S. " On the drag reduction in a mirobubble-laden spatially-developing turbulent boundary layer", **ONR workshop on Dynamics of Bubbly Flows,** Reston, VA, April 4-5, 2005.

A57 Elghobashi, S. " Reynolds number effect on drag reduction in a microbubble-laden spatially-developing turb. boundary layer", **Euromech Conference on Hydrodynamics of bubbly flows- [Invited Lecture]**- Lorentz Center, Leiden, the Netherlands, June 6-8, 2005.

A58 Elghobashi, S. "On drag reduction in a microbubble-laden spatially-developing turbulent boundary layer", **European Science Foundation- Challenging Turbulent Lagrangian Dynamics, [Invited Lecture]**- Castel Gandolfo, Italy, Sept. 1-4, 2005.

A59 Elghobashi, S. "On drag reduction in a microbubble-laden spatially-developing turbulent boundary layer", **Thirteen IUTAM Advanced School & Workshop, Particle Dispersion in Turbulent Flows, [Invited Lecture I]**- CISM, Udine, Italy, September 12-16, 2005.

A60 Elghobashi, S. " Reynolds number effect on drag reduction in a microbubble-laden spatially-developing turb. boundary layer", **Thirteen IUTAM Advanced School & Workshop, Particle Dispersion in Turbulent Flows, [Invited Lecture II]**- CISM, Udine, Italy, September 12-16, 2005.

A61 Ferrante, A. and Elghobashi, S. " Effects of microbubbles on the Taylor-Green vortex flow" , **58th Annual Meeting of American Physical Society,** Div. Fluid Dynamics,Chicago, IL, November 2005. Published in **Bulletin of APS, Vol. 50, p.130, 2005.**

A62 Elghobashi, S. and Ferrante, A. " Reynolds number effect on drag reduction

in a microbubble-laden spatially-developing turbulent boundary layer " , **58th Annual Meeting of American Physical Society,** Div. Fluid Dynamics,Chicago, IL, November 2005. Published in **Bulletin of APS, Vol. 50, p.132, 2005.**

A63 Elghobashi, S. " On the accuracy of the two- fluid formulation in DNS of a microbubble-laden turbulent boundary layer", **ONR 2006 Ship Wave-breaking and Bubble Wake Review,** Caltech, Pasadena, CA, March 29-30, 2006.

A64 Ferrante, A. and Elghobashi, S. " On the accuracy of the two-fluid formulation in DNS of bubble-laden turbulent boundary layers" , **59th Annual Meeting of American Physical Society, Div. Fluid Dynamics,** Tampa, FL, November 2006. Published in Bulletin of APS, Vol. 51, 2006.

A65 Elghobashi, S. " DNS of the two-way interactions between dispersed solid particles and turbulent flows", **Workshop on multiphase turbulence: Dust storms, erosion, hurricanes and tornadoes, [Invited Lecture], Xian, China,** July 16-18, 2007.

A66 Ferrante, A. and Elghobashi, S. " Fully resolved DNS of freely moving finite-size particles in decaying isotropic turbulence" , **60th Annual Meeting of American Physical Society, Div. Fluid Dynamics,** Salt Lake City, UT, November 2007. Published in Bulletin of APS, Vol. 52, 2007.

A67 Cleckler,J., Liu, F. and Elghobashi, S. " Aerosol particle motion induced by non-linear sound waves" , **61th Annual Meeting of American Physical Society, Div. Fluid Dynamics,** San Antonio, Texas, November 2008. Published in Bulletin of APS, Vol. 53, 2008.

A68 Elghobashi, S. "On the two-way interactions between dispersed solid particles and turbulent flows", **European Workshop on Direct and Large-Eddy Simulation, Keynote Lecture,** Trieste, **Italy,** Sept. 8-10, 2008.

A69 Lucci, F., Ferrante, A. and Elghobashi, S. " DNS of fully resolved spherical particles dispersed in isotropic turbulence " , **61th Annual Meeting of American Physical Society, Div. Fluid Dynamics,** San Antonio, Texas, November 2008. Published in Bulletin of APS, Vol. 53, 2008.

A70 Elghobashi, S. " On the two-way interactions between dispersed particles and turbulent flows ",**[Invited Lecture], March 2009 Meeting of American Physical Society** Pittsburgh, PA . Published in Bulletin of APS, Vol. 54, 209, March 18, 2009.

A71 Elghobashi, S. " The physical mechanisms of two-way interactions between dispersed particles and turbulent flows", **Workshop on Clouds and Turbulence Institute for Mathematical Sciences,** Imperial College, **[Invited Lecture],** London, **England,**

March 23-25, 2009.

A72 Elghobashi, S. " How do inertial particles modify isotropic turbulence ?" **International Workshop- Solving the Riddle of Turbulence: What, Why, and How?** Max Planck Institute for Dynamics and Self-Organization, **[Invited Lecture]**, Göttingen, **Germany,** May 6-9, 2009.

A73 Elghobashi, S. "How do inertial particles modify isotropic turbulence ?" **International Symposium on Turbulence", [Invited Lecture]**, Peking University, **Beijing, China,** Sept. 21-25, 2009.

A74 Lucci, F., Ferrante, A. and Elghobashi, S. " On the effects of Taylor-lengthscale size particles on isotropic turbulence ", **62nd Annual Meeting of American Physical Society, Div. Fluid Dynamics,** Minneapolis, Minnesota. Published in Bulletin of APS, Vol. 54, No. 19, p. 159, November 20-23, 2009.

A75 Lucci, F., Ferrante, A. and Elghobashi, S. " Is Stokes number an appropriate indicator for turbulence modulation by particles of Taylor-length-scale size? ", **63nd Annual Meeting of American Physical Society, Div. Fluid Dynamics,** Long Beach, California. Published in Bulletin of APS, Vol. 55, No. 16, p. 150, November 20-23, 2010.

A76 Cleckler, J., Liu, F. and Elghobashi, S. " Numerical simulation of particle dispersion in an acoustic field ", **63nd Annual Meeting of American Physical Society, Div. Fluid Dynamics,** Long Beach, California. Published in Bulletin of APS, Vol. 55, No. 16, p. 319, November 23, 2010.

A77 Lucci, F., L'Vov, V., Ferrante, A. and Elghobashi, S. " On the Lagrangian Power Spectrum of Turbulence Energy in Isotropic Turbulence ", **64th Annual Meeting of American Physical Society, Div. Fluid Dynamics,** Baltimore, MD , Published in Bulletin of APS, Vol. 56, No. 18, p. 80, November 20-22, 2011.

A78 Wang, Y. and Elghobashi, S. " Direct numerical simulation of the flow in the pediatric upper airway ", **34th Annual Int. Conf. of the IEEE Engineering in Medicine & Biology (EMB) Society,** San Diego, CA, August 28-September 1, 2012.

A79 Wang, Y. and Elghobashi, S. " Direct numerical simulation of the flow in the human upper airway ", **65th Annual Meeting of American Physical Society, Div. Fluid Dynamics,** San Diego, CA , Published in Bulletin of APS, Vol. 57, No. 17, p. 333, November 18-20, 2012.

A80 Wang, Y. and Elghobashi, S. " On locating the obstruction in the human upper airway,Direct numerical simulation ", **66th Annual Meeting of American Physical Society, Div. Fluid Dynamics,** Pittsburgh, PA, November 24-26, 2013.

A81 Y. Wang, L. Oren, E. Gutmark a and S. Elghobashi, " DNS and PIV measurements of the flow in a model of the human upper airway", **67th Annual Meeting of American Physical Society, Div. Fluid Dynamics**, San Francisco, CA, November 23-25, 2014.

Technical Reports

Yeh, G.C.K. and Elghobashi, S.E., "A Two-Equation Turbulence Model for a Dispersed Two-Phase Flow with Variable Density Fluid and Constant Density Particles", Defense Nuclear Agency Report DNA-TR-86-42, 1986.

Elghobashi, S.E. and Rizk, M.A., "The Effect of Solid Particles on the Turbulent Flow of a Round Gaseous Jet: A Mathematical and Experimental Study", DOE/PC,30303-5, December (1983).

Wassel, A.T., Elghobashi, S.E., and Wenger, R.S., "Analysis of the Sea Water Systems of Ocean Thermal Energy Conversion Pilot Plants", SAI Report No. 82R-018-LA, October (1982).

Bellan, J. and Elghobashi, S.E., "Present and Projected Status of Computer Modeling in Furnace and Boiler Technology', US DOE, Jet Propulsion Lab. Report, Nov. (1982).

Elghobashi, S.E., Lockwood, F.C. and Naguib, A.S., "The Calculation of Combustion Processes", Imperial College Mech. Engr. Dept., HTS/74/8, (1974).

Elghobashi, S.E., Pun, W.M., "A Theoretical and Experimental Study of Turbulent Diffusion Flames in Cylindrical Chambers", Imperial College, Mech. Engr. Dept., HTS/74/3, (1974).

Elghobashi, S.E., "Concentration Fluctuations in Isothermal Turbulent Confined Jets", Imperial College, Mech. Engr., HTS/75/23, (1975).

Elghobashi, S.E., "Prediction of the Three Dimensional Flow and Radiation Heat Transfer Inside a Cylindrical Glass Furnace", for Corning, (1977).

Elghobashi, S.E., "Prediction of the Three Dimensional Flow Inside a Liquid- Metal Fast-Breeder Reactor Steam Generator", for Westinghouse, (1978).

Elghobashi, S.E., "Prediction of the Flow and the Concentration of CO and NO_x inside a Burning Cigarette", for Philip Morris, (1977).

Elghobashi, S.E., "Prediction of the Flow Around the Earth and the Influence of Temperature Gradients on Both Hemispheres", for NASA Marshall, (1977).

Elghobashi, S.E., "Prediction of the Flow Inside a Crystal-Growth Device at Near-Zero Gravity", for NASA Marshall, (1978).

Elghobashi, S.E., "Prediction of the Effects of Low Gravity and Heat Transfer on the Trajectories of Blood Cells in an Electrophoresis Chamber", for NASA Marshall, (1978).

Elghobashi, S.E., "Prediction of the Flow and Electrical Properties of a Rocket Exhaust Plume", for US Air Force, (1978).

Elghobashi, S.E., Spalding, D.B. and Thyagraja, A., "Prediction of Three Dimensional Supersonic Flow of a Conical Body Interacting with a Plane Blast Wave", prepared for Ballistic Missile Defense Advance Technology Center, Huntsville, (1976).

Elghobashi, S.E., "Prediction of Transient Flow and Heat Transfer in 155 MM Gun Barrel and its Exhauster", prepared for Rheinmetall, West Germany (1976).

Elghobashi, S.E., "Prediction of Three Dimensional flow and Chemical Reaction in a Can Combustor with Fuel Spray", prepared for Airesearch Co. of Arizona (1976).

Elghobashi, S.E., Spalding, D.B. and Srivatsa, S.K. "Prediction of Three Dimensional Flow in a Hall-Cell Aluminum Smelter", prepared for ALCOA (1975).

Elghobashi, S.E., Moult, A. and Spalding, D.B., "Prediction of Compressible Flow in the Combustion Chamber of a Solid-Propellant Rocket" prepared for Societe National des Poudres et Explosifs, France (1975).

Elghobashi, S., Rosten, H. and Spalding, D.B.," Effects of gravity on Methane-air combustion", **NASA-CR 2671**, (1974).

Elghobashi, S., Pratt, D.T., Runchal, A.K., Spalding, D.B. and Srivatsa, S.K. " Unsteady combustion of fuel spray in jet engine afterburners, The CID4 computer program," CHAM 551/1, (1975).

Elghobashi, S., Spalding, D.B. and Srivatsa, S.K., " Prediction of hydrodynamics and chemistry of confined turbulent methane-air flames with attention to formation of oxides of nitrogen,"**NASA CR-135179**, (1977).

Elghobashi, S. and Spalding, D.B., " Equilibrium chemical reaction of supersonic hydrogen-air jets (The ALMA computer program)", **NASA CR-2725**, (1977).

Invited Research Presentations (1983- Present)

"How do dispersed inertial particles modify turbulent flows ?" **École Polytechnique,** The Hydrodynamics Laboratory (LadHyX), **Palaiseau, France,** June 14, 2013.

"How do dispersed inertial particles modify turbulent flows ?" **University of California, San Diego,** Mechanical and Aerospace Engineering Dept., June 3, 2013.

"Direct numerical simulation of the flow in the upper airway via lattice Boltzmann method" **National Institute of Health,** Bethesda, MD, April 29, 2013.

"On the physical mechanisms of drag reduction in a spatially-developing turbulent boundary layer laden with microbubbles " **École Normal Supérieur, Paris, France,** March 17, 2011.

."Direct numerical simulation of the flow in the upper airway via lattice Boltzmann method" **National Institute of Health,** Bethesda, MD, Feb. 24, 2011.

"Turbulence modulation by dispersed inertial particles" Mech. Eng. Dept., **Univ. of California, Berkeley,** February 11, 2011.

" On the two-way interactions between dispersed particles and turbulent flows" **School of Engineering and Mathematical Sciences, City University, London, England,** March 26, 2009.

"On the effects of finite-size solid particles on decaying isotropic turbulence", **Institut de Mècanique des Fluides de Toulouse, IMFT, Toulouse, France,** June 28, 2007.

"On the physical mechanisms of drag reduction in a spatially-developing turbulent boundary layer laden with microbubbles " **Ecole Polytechnique,** The Hydrodynamics Laboratory (LadHyX), **Palaiseau, France,** June 26, 2007.

"Turbulence modification in flows laden with particles or bubbles" **The Johns Hopkins University,** Mechanical Engineering Department, February 15, 2007.

" Direct simulation of turbulent flows laden with particles or bubbles", **Invited Lecture, CIEMAT : Research Centre for Energy, Environment and Technology, Madrid, Spain, June 21, 2006.**

"On drag reduction in a spatially-developing turbulent boundary layer laden with microbubbles", **Department of Mechanics and Aeronautics, University of Rome "La Sapienza", Rome,, Italy,** September 5, 2005.

"On the drag reduction in a mirobubble-laden spatially-developing turbulent boundary

layer," **School of Mechanical and Aerospace Engineering, Center for Turbulence and Flow Control Research, Seoul National University, Seoul, South Korea**, May 27, 2005.

"On the physical mechanisms of drag reduction in a mirobubble-laden turbulent boundary layer", **Department of Mechanical Engineering, University of Tokyo, Japan, June 7, 2004.**

"On the physical mechanisms of drag reduction in a spatially-developing turbulent boundary layer laden with microbubbles", **Mech. Eng. Dept., Univ. California, Santa Barbara, California**, February 14, 2004.

"Recent advances in DNS of particle-laden turbulent flows ", **Institute for Scientific Computing Research, Lawrence Livermore Research Laboratory, Livermore, California** , August 7, 2003.

"DNS of turbulent flows laden with particles ", **Institute for Scientific Computing Research, Lawrence Livermore Research Laboratory, Livermore, California** , March 27, 2003.

" On the physical mechanisms of modifying the structure of turbulent homogeneous shear flows by dispersed particles", **Mechanical Engineering Dept., Stanford University, Stanford, California**, October 30, 2001.

"Recent Advances in DNS of Turbulent Flows Laden with Particles, Droplets or Bubbles", **Universite Pierre et Marie Curie, Paris, France**, September 19, 2001.

"Recent advances in direct numerical simulations (DNS) of turbulent shear flows laden with particles ", **Institute for Scientific Computing Research, Lawrence Livermore Research Laboratory, Livermore, California** , May 4, 2001.

"Recent Advances in DNS of Turbulent Flows Laden with Particles, Droplets or Bubbles", **The Aerospace Corporation, Los Angeles, California**, April 17, 2001.

"Recent advances in direct numerical simulations (DNS) of turbulent shear flows laden with particles ", **Institute for Scientific Computing Research, Lawrence Livermore Research Laboratory, Livermore, California** , May 4, 2001.

" On the physical mechanisms of modifying the structure of turbulent homogeneous shear flows by dispersed particles ", **ETH, Zürich, Switzerland**, October 4, 2000.

" Recent advances in direct numerical simulations (DNS) of turbulent shear flows laden with particles ", **Paul Scherer Institute, Villigen, Switzerland**, October 3, 2000.

" Recent advances in direct numerical simulations (DNS) of turbulent shear flows laden with particles and bubbles", **Mechanical Engineering Department, Imperial College, London**, April 6, 2000.

" Recent advances in direct numerical simulations (DNS) of turbulent shear flows laden with particles and bubbles", **Mechanical and Aerospace Engineering Department, Univ. California, San Diego**, March 15, 2000.

" Direct numerical simulation of particle-laden flows: the trajectory and two-fluid approaches", **Dept. of Mechanical Engineering, Univ. of Illinois, Urbana-Champaign**, November 9, 1999.

" Evolution of flame surface in buoyant and nonbuoyant turbulent nonpremixed reactions", **Graduate Aeronautical Laboratories, California Institute of Technology**, January 16, 1998.

" How do particles modify the turbulence energy in a homogeneous shear flow ?", **Department of Chemical Engineering, Univ. of California, Santa Barbara**, April 16, 1997.

" Direct numerical simulation of particle-laden homogeneous turbulent shear flows", **CEA : Atomic Energy Commision - Military Applications Division**, Bordeaux, France, April 2, 1997.

" Mathematical models of particle-laden flows", **CEA : Atomic Energy Commision - Military Applications Division**, Bordeaux, France, April 2, 1997.

" DNS of surface topology of turbulent nonpremixed flames ", **CEA : Atomic Energy Commision - Military Applications Division**, Bordeaux, France, April 2, 1997.

"Effects of buoyancy on turbulent diffusion flames", Dept. of Mechanical Engineering, **Yale University**, June 10, 1996.

"Particle dispersion and turbulence modification in a homogeneous shear flow"; Dept. of Mechanical Engineering, **California Institute of Technology**, April 23, 1996.

" Particle dispersion and turbulence modulation in a homogeneous shear flow", Aerospace Engineering Dept., **University of Southern California**, October 4, (1995).

" DNS of particle dispersion in homogeneous shear turbulence" **Institut de Mecanique des Fluides de Toulouse, Toulouse, France**, September 12, (1995).

" DNS of a turbulent diffusion flame under different gravity conditions" **Institut de Mecanique des Fluides de Toulouse, Toulouse, France**, September 12, (1995).

" DNS of particle dispersion in homogeneous shear turbulence" **Technical University of Delft, Delft, Netherlands**, September 7, (1995).

" DNS of a turbulent diffusion flame under different gravity conditions" **Technical University of Delft, Delft, Netherlands**, September 7, (1995).

" On the two-way interaction between homogeneous turbulence and dispersed solid particles",**Naval Command, Control and Ocean Surveillance Center, San Diego, CA**, Oct. 19, 1993.

" On the two-way interaction between homogeneous turbulence and dispersed solid particles", **Arizona State University, Tempe, Arizona**, Oct. 8, 1993.

" Direct numerical simulation of particle dispersion and turbulence modulation in homogeneous turbulence",**NATO Advanced Research Workshop on Chaotic Advection, Tracer Dynamics, and Turbulent Dispersion, Alessandria, Italy**, May 24-28, 1993.

" On predicting particle-laden turbulent flows", Workshop on turbulence in particulate multiphase flow,**Fluid Dynamics Laboratory, Battelle Pacific Northwest Laboratory, Richland, WA**, March 22, 1993.

" On the two-way interaction between homogeneous turbulence and dispersed solid particles", **AMES Dept. Univ. of California, San Diego**, February 5, 1993.

" On the two-way interaction between homogeneous turbulence and dispersed solid particles",**NASA Langley Research Center**, December 14, 1992.

" On the modification of energy spectrum of homogeneous turbulence by dispersed solid particles",**Department of Mathematics, UCI**, May 21, 1992.

" The two-way coupling between solid particles and homogeneous decaying turbulence", **Mechanical and Aerospace Engineering Department, Princeton University**, August 23, 1991.

" Direct simulation of particle-laden homogeneous turbulence",**Los Alamos National Laboratory**, May 25, 1991.

"The effect of turbulence on the propagation of an electromagnetic wave in a compressible turbulent boundary layer", Workshop on Aerothermal Technology Development,**U.S. Strategic Defense Command , Huntsville, Alabama**, June 13, 1991.

"Direct numerical simulation and closure modelling of particle-laden turbulent flows", Workshop on Turbulence Simulation and Modelling , **NASA-Marshall, Huntsville,**

Alabama, April 14-15, 1991.

"Direct numerical simulation of particle dispersion in sheared and unsheared homogeneous turbulence", **Mechanical Engineeing Department, University of Southern California,** March 1, 1990.

"Direct numerical simulation and modelling of particle-laden turbulent flows", **German Aerospace Organization (DLR), Munich, Germany,** December 4,1989.

"Direct numerical simulation of particle dispersion in homogeneous turbulent flows", **University of Kaiserslautern , West Germany,** December 5,1989.

"Direct numerical simulation of particle dispersion in isotropic and sheared turbulent flows", **Institut de Mecanique des Fluides, Toulouse, France,** December 6,1989.

"Direct numerical simulation of particle dispersion in homogeneous turbulent flows", **University of Rouen, France,** December 7,1989.

"Direct numerical simulation and modelling of particle-laden turbulent flows",**Shell Conference on Computational Fluid Dynamics, Apeldoorn, The Netherlands,** December 11,1989.

"Direct numerical simulation of particle dispersion in homogeneous turbulent flows", **Norway Institute of Technology, Trondheim, Norway,** December 15,1989.

"Direct numerical simulation of particle dispersion in grid-generated turbulence", Workshop on droplets and sprays,**AFOSR and ONR Contractors Meeting, Ann Arbor, Michigan,** June 21,1989.

"Direct numerical simulation of particle dispersion and chemical reaction in turbulent flows",**G.M. Research Laboratory, Thermal Science Department, Warren, Michigan,** June 22,1989.

"Direct numerical simulation of stratified turbulent homogeneous shear flow", **Idaho National Engineering Laboratory, Idaho Falls,** September 8,1988.

"Direct numerical simulation of stratified turbulent homogeneous shear flow",**Center for Microgravity and Materials Research, University of Alabama, Huntsville** , August 5, 1988.

"Direct simulation of stable stratified turbulent homogeneous shear flows", Third International Symposium on Stratified Flows, **California Institute of Technology,** February 3-5, 1987.

"Direct simulation of the passive-scalar mixing layer",**Institut de Mecanique des Fluides, Toulouse, France,** September 11, 1987.

"Direct simulation of stratified homogeneous turbulent shear flow",**Department of Aerospace Engineering, University of Southern California,** October 8, 1986.

"Direct simulation of stratified homogeneous turbulent shear flow", **Institut de Mecanique Statistique de la Turbulence, Marseille, France,** October 22, 1986.

"Direct simulation of homogeneous turbulent shear flow", **Mechanical Engineering Department, University of California, Irvine,** July 22, 1986.

"Direct simulation of stratified homogeneous turbulent shear flow",**AMES Department, University of California, San Diego,** February 3, 1986.

"Direct simulation of turbulent shear flow with buoyancy",**Jet Propulsion Laboratory, California Institute of Technology,** May 30, 1986.

"Direct numerical simulation of a turbulent homogeneous shear flow with buoyancy", **Mechanical Engineering Dept., University of California, Irvine,** October 18, 1985.

"Direct simulation of turbulent homogeneous shear flow", **DFVLR, Institute of Atmospheric Physics, Oberpfaffenhofen, West Germany ,** June 21, 1985.

"Prediction of the turbulent jet laden with vaporizing droplets" **Dept. of Fluid Mechanics, University of Erlangen, West Germany,** May 22,1985.

"Experimental study of the turbulent jet laden with particles", **University of the German Armed Forces, Aerospace Department, Munich, West Germany,** February 7,1985.

"Measurement and prediction of the turbulent two-phase jet", **University of Karlsruhe, Mechanical Engineering Dept.,** December 13,1984.

"Prediction of the turbulent jet laden with solid spherical particles",**DFVLR, Institute of Atmospheric Physics, Oberpfaffenhofen, West Germany ,** December 5, 1984.

"Recent developments in mathematical modeling of dispersed two- phase flows", presented at the Mechanical Engineering Dept., Technical University of Munich, West Germany, November 27,1984.

"Recent developments in mathematical modeling of dispersed two- phase flows", presented at the **Mechanical Engineering Dept., University of California, Berkeley,** March 20, 1984.

"Effects of dispersed two-phase flows on turbulence structure", **Office National d'Etudes et de Recherches Aerospatiales (ONERA), Paris, France,** September 19, 1983.

"Turbulence modulation in a turbulent two-phase jet : theory and experiment", Mechanical Engineering Department, **University of Kaiserslautern, West Germany,** September 16, 1983.

"Passive-scalar time-scales in turbulent flows", **DFVLR, Institute of Atmospheric Physics, Oberpfaffenhofen, West Germany** , September 15, 1983.

"Mathematical models of temperature variance and time-scales for the thermal mixing layer ", **Institut de Mecanique Statistique de la Turbulence, Marseille, France,** July 8, 1983.

"Experimental and theoretical study of dispersed two-phase turbulent jets", **Institut de Mecanique des Fluides, Toulouse, France,** July 6, 1983.

EXHIBIT DX4

TO DECLARATION OF BENJAMIN W. HULSE IN SUPPORT OF DEFENDANTS' MOTION FOR RECONSIDERATION OF THE COURT'S DECEMBER 13, 2017 ORDER ON GENERAL CAUSATION

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LETTER TO THE EDITOR

Active warming systems to maintain perioperative normothermia in hip replacement surgery

Madam,

In response to Moretti *et al.*'s article 'Active warming systems to maintain perioperative normothermia in hip replacement surgery: a therapeutic aid or a vector of infection?', the National Institutes of Health (NIH) used computational fluid dynamics (CFD) and particle-tracking methodology to assess whether a forced-air patient-warming system increases the risk of nosocomial infections at the surgical wound site.[1] NIH analysed laminar airflow disruption and room airflow patterns to determine the effect of squame impingement from personnel surrounding the operating table as a source of surgical wound infection.

The literature indicates that a forced-air warmer system may disturb the operating room laminar airflow and increase the risk of nosocomial infections. Memarzadeh *et al.* used advanced numerical modelling and empirical data to evaluate the effects of room parameters on minimising surgical site contamination risk from specific particulate sources.[2,3] Their work shows that <1% of particles hitting the surgical site from the anaesthesiologist location are due to the relative dominance of the thermal plume caused by the surgical site.[3]

Using colony-counting methodology to determine settling of squames on the surgical site, Moretti *et al.* concluded that the body-warming system does not pose a risk of nosocomial infections and that the increased bacterial load found after application of a body warming system is comparable to, or lower than, the load present at the time of placement of the patient on the operating table.[1]

Memarzadeh explains that turbulent airflow in a ventilated room transports the squames by both airflow convection and turbulent diffusion. The influence of the squames' motions and temperatures on the fluid flow parameters is negligible because squames are sufficiently light and their volume flow rate is substantially lower than those of the fluid stream. The distributions of air velocities and the turbulent parameters from the CFD simulation output are directly applied to predict the path of the airborne squames in convection and diffusion processes. The particle motion in the air obeys an equation, as described further in our full publication.

The NIH analysis includes heat-generating factors and ventilation factors. The air supply temperature was determined by the average room air temperature (70°F) assuming 15 and 20 air changes per hour (ACH).

NIH made observations with the air warmer on and off compared with two ventilation flow rates. The squames are 25 μm by 3–5 μm thick. Approximately 30 000 total squames were released from the head and arms of the anaesthesiologist location and tracked for 1 h. The number of squames deposited on the patient surface was compared for both scenarios.

Simulation results of flow fields and particle tracking show velocity plots at the vertical plane cutting through the centre of the operating table with 20 ACH for the two scenarios. Flow patterns in both plots are similar except that the downward velocity from ceiling laminar diffuser is slightly less strong with the forced-air warmer operating than when the air warmer is off. Similar flow patterns are observed 1 h after the squames are released from the sources. Since the operating air warmer system adds hot air but also dissipates heat to the region around the bed, the air temperature is apparently higher than when the air warmer is off. The squame plots show that particles are cleaned away from the patient by the airflow from the laminar diffuser no matter if the forced air warmer is on or off. The percentage of squames deposited on the patient was zero both when the forced air warmer was on or off. The percentage of squames vented at the exhausts was 5.58% when the forced air warmer was operating and 5.26% when it was off. The percentage of squames being vented out is low because they stick to the solid surfaces during the 1 h tracking before reaching the return grilles.

NIH concludes that in both scenarios, there is zero percent deposition on the patient for the contaminant sources and the heat generated by the patient provides some protection. Although squames from the anaesthesiologist location move upwards due to thermal plume and away from the surgical site, supply flows largely dictate airflow pattern. When the forced-air warmer is operating, the downward velocity from ceiling laminar diffuser is slightly less strong than when it is off. With same supply air temperature, the air temperature around the surgical table is warmer when the forced-air warmer is operating. Forced-air warmers seem to cause minimal disruption to laminar airflow systems that help protect the surgical site from contaminated particles sourced from surgical staff.

This investigation validates Moretti *et al.*'s conclusion that forced-air warming technology does not increase the risk of surgical wound infection. Further, if the operating room ventilation system is designed properly, contaminating particles from staff around the patient will not impinge on the surgical wound due to 'thermal plume' dynamics.

Conflict of interest statement
None declared.

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References

1. Moretti B, Larocca AMV, Napoli C, *et al.* Active warming systems to maintain perioperative normothermia in hip replacement surgery: a therapeutic aid or a vector of infection? *J Hosp Infect* 2009;**73**:58–63.
2. Memarzadeh F, Manning A. Comparison of operating room ventilation systems in the protection of the surgical site. *ASHRAE Trans* 2002;**108**(Pt 2).
3. Memarzadeh F, Jiang Z. Effect of operation room geometry and ventilation system parameter variations on the protection of the surgical site. *Indoor Air Quality (IAQ)*; 2004.

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EXHIBIT DX5

TO DECLARATION OF BENJAMIN W. HULSE IN SUPPORT OF DEFENDANTS' MOTION FOR RECONSIDERATION OF THE COURT'S DECEMBER 13, 2017 ORDER ON GENERAL CAUSATION

Anesthesia Patient Safety Foundation

Section Editor: Sorin J. Brull

Patient Warming Excess Heat: The Effects on Orthopedic Operating Room Ventilation Performance

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BACKGROUND: Patient warming has become a standard of care for the prevention of unintentional hypothermia based on benefits established in general surgery. However, these benefits may not fully translate to contamination-sensitive surgery (i.e., implants), because patient warming devices release excess heat that may disrupt the intended ceiling-to-floor ventilation airflows and expose the surgical site to added contamination. Therefore, we studied the effects of 2 popular patient warming technologies, forced air and conductive fabric, versus control conditions on ventilation performance in an orthopedic operating room with a mannequin draped for total knee replacement.

METHODS: Ventilation performance was assessed by releasing neutrally buoyant detergent bubbles ("bubbles") into the nonsterile region under the head-side of the anesthesia drape. We then tracked whether the excess heat from upper body patient warming mobilized the "bubbles" into the surgical site. Formally, a randomized replicated design assessed the effect of device (forced air, conductive fabric, control) and anesthesia drape height (low drape, high drape) on the number of bubbles photographed over the surgical site.

RESULTS: The direct mass-flow exhaust from forced air warming generated hot air convection currents that mobilized bubbles over the anesthesia drape and into the surgical site, resulting in a significant increase in bubble counts for the factor of patient warming device ($P < 0.001$). Forced air had an average count of 132.5 versus 0.48 for conductive fabric ($P = 0.003$) and 0.01 for control conditions ($P = 0.008$) across both drape heights. Differences in average bubble counts across both drape heights were insignificant between conductive fabric and control conditions ($P = 0.87$). The factor of drape height had no significant effect ($P = 0.94$) on bubble counts.

CONCLUSIONS: Excess heat from forced air warming resulted in the disruption of ventilation airflows over the surgical site, whereas conductive patient warming devices had no noticeable effect on ventilation airflows. These findings warrant future research into the effects of forced air warming excess heat on clinical outcomes during contamination-sensitive surgery. (Anesth Analg 2013;117:406–11)

Operating room (OR) ventilation has been recognized, historically, as an important component of a multifaceted infection reduction strategy in orthopedics. Starting with the work of Sir John Charnley in the 1960s,[1] 20 years of research established the benefits of using sophisticated ventilation systems to create localized zones of highly filtered air over the surgical site. Clinically, these systems were shown to reduce surgical site microbial exposure[2] and led to the United Kingdom commissioning the first and only randomized clinical trial, which demonstrated a significant reduction in orthopedic infection rates.[3] Recently, though, a number of national studies have shown no infection reduction benefits.[4–6] These results question the value of sophisticated ventilation systems. Although the cause for such failures is presently unknown, changes have been made to OR equipment that may affect ventilation performance; notable among them the introduction of forced air patient warming in the 1990s.

Patient warming is a recognized and necessary standard of surgical care, with warmed patients having better outcomes through reduced blood loss, improved wound healing, reduced duration of hospital stay, improved survival, and reduced surgical site infection rates for "dirty" (colorectal) surgery.[7,8] However, patient warming systems incidentally release excess heat that is not absorbed by the patient. This excess heat naturally rises and may disrupt the intended ceiling-to-floor OR ventilation airflows. Thus, potential for ventilation disruption may be proportional (among many other factors) to the amount of excess heat emitted, which depends on the choice of patient warming technology.[9]

Two general classes of patient warming technology are used intraoperatively. The first, forced air, warms by distributing heated air (up to 43°C) under the surgical

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drapes and over the patient in a large envelope.[10] The second, conductive blankets, uses a resistive heating element or hot water jacket (for heated water blankets) to directly apply heat to the patient's skin.[11] Because conductive blankets are localized in their application, they tend to have higher thermal efficiencies and contribute less excess heat to the environment than forced air.[12] Therefore, in this study, we chose to evaluate the effects of both patient warming technologies versus control (no warming) on ventilation performance. The study was conducted in a standard orthopedic OR having ceiling-to-floor displacement ventilation with a mannequin draped for total knee replacement having upper body patient warming applied. Changes in ventilation airflow patterns were assessed using neutrally buoyant detergent bubbles.

METHODS

OR Characteristics

Experiments were performed in a downward displacement ventilation OR used for orthopedic surgery at the University of Minnesota Hospital (Minneapolis, MN). Ceiling-to-floor airflows are generated by a 2.43 × 2.43 m continuous grid (100% coverage) of diffuser panels over the OR table, each of which contains a final point-of-use high-efficiency particulate air (HEPA) filter. Supply air is centrally pressurized, prefiltered, and then ducted to the individual ORs. The OR used for these experiments received a supply airflow of 51.5 m^3/min, resulting in 19.7 air changes per hour; minimum requirements for hospital ventilation are 15 air changes per hour.[13] Airflow balance is certified yearly. Surgical lighting was provided by 2 Chromophare D650 Plus overhead lights (Berchtold Corporation, Charleston, SC), which were turned off during experiments. OR temperature was set to 20°C.

Airflow Visualization Procedures

High-intensity lighting was used to illuminate neutrally buoyant detergent bubbles having a 4-mm average diameter (referred to herein as "bubbles"). Bubbles were produced by a generator (Sage Action, Ithaca, NY), which used a helium and air supply. The equipment filters the bubbles using a centrifugal classifier that only allows bubbles of neutral buoyancy to pass; those heavier or lighter are discarded. The bubble generator is specifically designed and validated for the visualization of air currents.[14] For photography, a digital camera (500D; Canon, Surrey, UK) was used, and shutter exposure time was set to 1/4 of a second for time-lapsed photography.

Total Knee Replacement Experimental Setup

A mannequin was laid in the supine position and draped in accordance with the standard draping protocol used by the hospital for knee replacement procedures. A perforated drape was used for the proximal limb, with a sterile stocking for the foot and distal limb (Fig. 1). An anesthesia provider dressed in surgical scrubs stood motionless at the head of the table behind the anesthesia/surgery drape. The anesthesia/surgery drape was either (1) clipped to IV poles and raised 0.75 m above the operating table (high-drape), or (2) clipped to IV poles and raised 0.25 m above the operating table (low-drape). The upper body warming device was introduced under the drape and was (1) a torso forced air blanket (Bair Hugger Model 540; Arizant Healthcare, Eden Prairie, MN), (2) a torso conductive fabric blanket (Hot Dog Model 8110; Augustine Temperature Management, Eden Prairie, MN), or (3) no warming device (control). The blankets were powered by standard controllers set to 43°C (forced air, Model 750, Arizant Healthcare; conductive fabric, Model WC02, Augustine Temperature Management) and affixed according to manufacturers' instructions. Bubbles were introduced at the head/neck of the mannequin to track under drape resident air movements in the region where the excess patient warming heat was being released. To ensure a consistent release point and direction for the bubbles exiting the generator, the diffuser cone was laid down on the OR head pad and aimed directly into the drape (perpendicular to the raised drape edge).

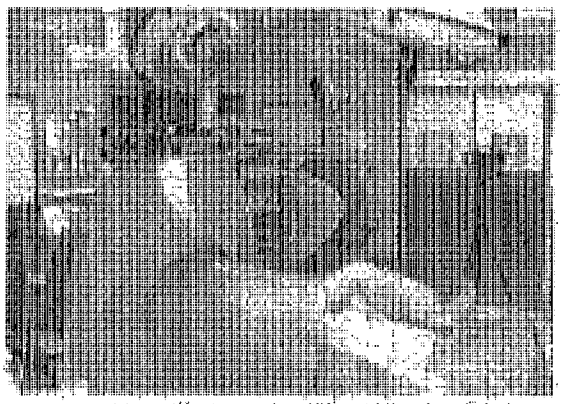

Figure 1. Total knee replacement setup showing high anesthesia drape position (A) and low anesthesia drape position (B).

Sampling Procedures

Bubble counts over the surgical site were measured using a sequence of 10 photographs taken at 10-second intervals for each experimental run. A 5-minute period was allowed between randomized experimental runs for conditions to equilibrate; all study data were collected on the same day. The number of bubbles reaching the surgical site was determined by counting the number of bubbles intersecting a vertical light curtain in a 0.75 × 0.75 m

Figure 2. 1, Definition of count region above the surgical site (dashed lines) showing neutrally buoyant detergent "bubbles," which appear as white dots (A) when they intersect the vertical light plane. Photograph is from the forced air warming and high drape experimental run. 2, View of bubbles exiting the diffuser end in still air (outside the operating room in a laboratory).

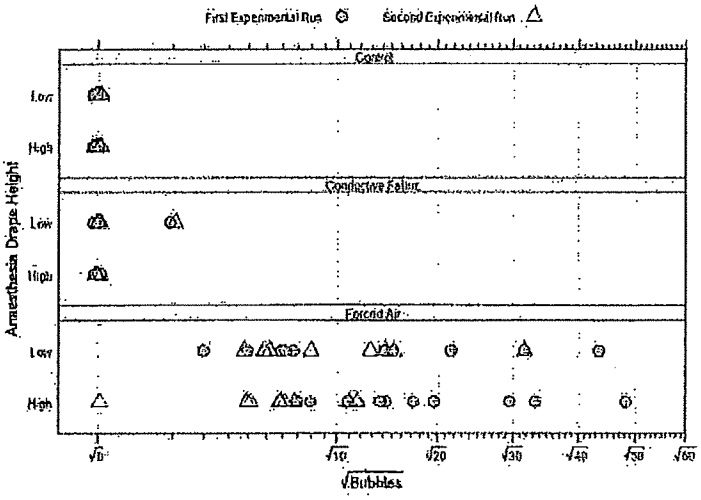

Figure 3. Bubble counts over the surgical site for each photograph (data are jittered to avoid overprinting). Ten photographs were taken for each experimental run.

region directly over the surgical site (Fig. 2). Additionally, time-lapse photography was performed to provide directional information on airflow patterns not captured in bubble count data.

Experimental Design

A replicated ($n = 2$) $2^2 3^1$ full factorial design was used to assess changes in bubble counts over the surgical site. The experimental factors considered were (1) anesthesia screen (low-drape or high-drape), and (2) patient warming device (conductive fabric, forced air, or no warming device) (control).

Statistical Analysis

A Poisson regression model for overdispersed data was fit having the sum of bubble counts for each experimental run (10 pictures) as the response and the factors identified in the experimental design as predictors plus an interaction term. A log-likelihood ratio test was used to determine the significance of the interaction term by comparing the full model versus an additive model with adjustment for overdispersion; if the interaction term was insignificant, a second set of tests for each additive parameter was performed using a log-likelihood ratio test comparing the parameter deleted additive model versus the full additive model with adjustment for overdispersion. Reported means and standard errors were computed using maximum likelihood parameter estimates and contrasts assuming asymptotic normality (Wald tests). P values correspond to 2-tailed tests and P values <0.05 were considered significant.

Results

Bubble Counts Over the Surgical Site

In viewing the raw bubble count data (Fig. 3), it is apparent that there is a large increase in the number of bubbles reaching the surgical site when forced air warming is in use versus either conductive fabric warming or control conditions. Furthermore, this increase seems to be independent of drape height.

Table 1. Poisson Bubble Count Model Parameters and Their Significance

Model parameter	P value
Drape height[a]	0.937
Patient warming device[a]	<0.001
Drape height × patient warming device[b]	0.980

[a] Computed using likelihood ratio deleted parameter tests from the additive model.
[b] Computed using a likelihood ratio comparing full and additive model.

Formal inference using Poisson regression (Table 1) revealed the only significant factor affecting sum of bubble counts to be patient warming device ($P < 0.001$); the factors of drape height ($P = 0.94$) and the interaction term between drape height and patient warming device ($P = 0.98$) were insignificant. With the full additive model (Fig. 4), the use of forced air warming was found to result in a predicted mean sum of bubble counts equal to 132.5 when averaged across both anesthesia drape heights; such a count represents a significant increase in the number of bubbles reaching the surgical site versus both conductive fabric warming ($P = 0.003$) and control conditions ($P = 0.008$), which had predicted mean sum of bubble counts equal to 0.48 and 0.01, respectively. Moreover, differences in the number of bubbles reaching the surgical site were not significantly different between conductive fabric warming and control conditions ($P = 0.87$).

Time-Lapse Photography

With forced air warming, convection current formation was detected in the space between the anesthesiologist's body and the anesthesia drape (Fig. 5). These convection currents were observed to mobilize resident air near the mannequin's head upward and over the topside of the anesthesia drape, which then spilled into the surgical site. Furthermore, the presence of an overhead surgical light had a significant impact on the dynamics of these convection currents; the recirculation zone extending below the light tended to magnify resident air mobilization into the

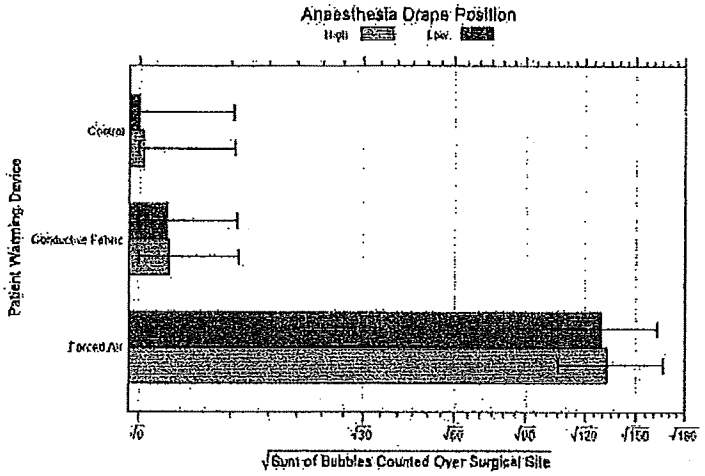

Figure 4. Predicted mean sum of bubble counts (±SEM). Predicted means and standard errors were computed from the full additive model with adjustment for overdispersion.

Figure 5. Time-lapse photography of forced air warming showing upward mobilization of neutrally buoyant detergent bubbles caused by hot air convection currents. Note: Bubble diffuser was moved from the experimental position (laid-down on operating room table) to better illustrate the effect for photography.

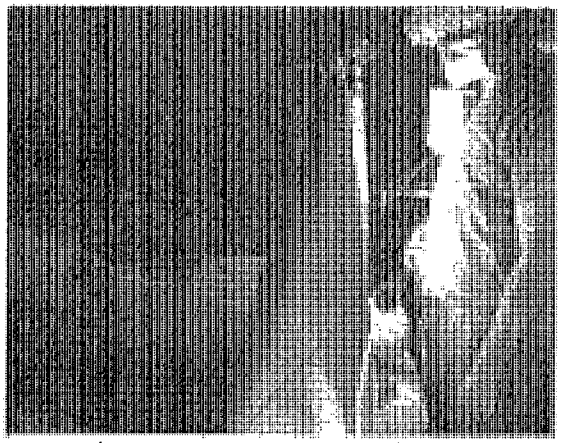

Figure 6. Time-lapse photography of conductive fabric warming showing no noticeable effect on ceiling-to-floor ventilation airflows (i.e., the neutrally buoyant detergent bubbles are swept down and away from the surgical site). Control conditions looked identical and, thus, are not shown separately. Note: Bubble diffuser was moved from the experimental position (laid-down on operating room table) to better illustrate the effect for photography.

surgical site by redirecting the upward convection currents into the light's "flow-shadow" and over the surgical site. As a note, the surgical lights were not moved over the course of the experiments and their setup is displayed in Figure 1.

In contrast, convection currents were not detected with conductive fabric warming (Fig. 6) and, therefore, there was no apparent upward mobilization of resident air. Instead, ventilation airflows were observed to follow the intended ceiling-to-floor path, sweeping contaminants down and away from the surgical site. Time-lapse photography of control conditions looked identical to those recorded with conductive fabric warming and, as such, are not displayed separately.

DISCUSSION

In this study, we sought to evaluate the effects of patient warming excess heat, using 2 fundamentally different technologies, forced air and conductive fabric, on OR ventilation performance. Under the above-explained experimental conditions, forced air warming was found to have a significant disruptive impact on clean airflow patterns over the surgical site, whereas conductive fabric warming had no noticeable effect versus controls. Moreover, forced air warming was found to establish convection currents that mobilized resident air from nonsterile areas (under the anesthesia drape) upward and into the surgical site. The clinical concern is that convection currents may mobilize under-drape contaminants into the surgical site and/or impede the ventilation systems' ability to clear contaminants from the surgical site. These concerns are most relevant for smaller airborne particles ≤10 μm, such as free-floating bacteria[15] and skin cell fragments,[16] having similar airborne characteristics to the neutrally buoyant detergent bubbles studied (i.e., appreciable suspension times).

The buoyancy-driven convection currents appeared to form in regions of localized ventilation disturbance caused

by surgical lighting, drapes, and personnel. For example, past research has identified surgical lighting to be a significant source of ventilation disruption through the downstream wake and concomitant recirculation zone.[14] In the present study, we were able to visualize this recirculation zone using bubbles and found it to extend approximately 1 m below each light. Such disruption was further magnified by the presence of a raised anesthesia drape, which created a still zone by blocking the natural passage of air out of the ventilation field. Lastly, the presence of an anesthesiologist behind the anesthesia drape added a final flow obstruction[17] and, ultimately, created a channel behind the drape in which ventilation airflows were nearly quiescent. Under these fragile conditions, the mass flow of forced air warming exhaust was sufficiently buoyant to push upward, over the top drape edge, and into the surgical site.

It is worth mentioning, however, that the observed disruption was dependent on our exact setup (i.e., arrangement of draping, lights, and personnel), which did not include the presence of instrument trays and a working surgical team. Thus, we are unsure of the exact degree of ventilation disruption that might occur in a working OR during orthopedic surgery. We can, however, state some observations regarding this extrapolation. First, surgical personnel and their associated movements lead to localized zones of ventilation disruption,[17] a factor that was identified as contributing to the formation of excess heat convection currents in this study. As such, removal of the surgical team from the experimental setup would most likely reduce the incidence of convection current formation. Second, instrument trays act as flow obstructions and would be expected to have a similar effect. Thus, similar ventilation systems, with respect to airflow, diffuser configuration, lighting, and draping arrangement, seem to be at risk for disruption with any surgical team/instrument tray configuration. Third, it should be noted that the head-end surgical light was positioned close to the raised anesthesia drape. This placement was attributable to the height of our surgeon (6 ft, 3 in), who needed sufficient head room to operate. Thus, for shorter surgeons, different results might be expected. Lastly, it was necessary to turn surgical lights off during the experiment to allow for consistent bubble counts in the intersecting light plane. Given that lighting heat sources tend to adversely affect ventilation performance,[14] our results should be considered conservative.

The most recent articles published on the association between patient warming excess heat and ventilation disruption present contradictory conclusions. Two studies conducted in the United Kingdom have characterized both the thermal basis[9] and airflow patterns[18] supporting the physics behind ventilation disruption in laminar flow ORs. In contrast, a published study in the Netherlands[19] found no evidence of ventilation disruption due to forced air excess heat when evaluated with the DIN 1946:2008-12 standard.[20] This discrepancy in findings is likely related to 2 primary differences in test methods.

First, the surgical lights were positioned in line with the OR table in both of the United Kingdom studies based on common clinical practice, whereas the lights were positioned to the sides of the OR table in the Netherlands study. Second, the United Kingdom study assessing airflow patterns evaluated the effect of patient warming excess heat on interior particle loads, defined as neutrally buoyant bubbles released (1) near the surgeon at floor level, and (2) under the anesthesia drape at the head of the OR table. With the Netherlands study, it is unclear whether the protective effect was assessed for outside particle loads (particles released on the periphery of the ventilation boundary) or inside loads (particles released by the surgeon).

Therefore, it seems that future research is warranted to characterize the clinical conditions under which forced air warming excess heat results in ventilation disruption during surgery. Careful attention should be given to the factors of draping, ventilation airflows, flow obstructions (lighting, instrument trays), and personnel movements, each of which has been identified as affecting this phenomenon. Preferably, this research would be conducted on a national basis covering orthopedic operations in both laminar flow and conventional ventilation environments, including infection-based end points (airborne bacteria, fomites, and/or joint sepsis rates) for an assessment of clinical risk.

DISCLOSURES

Name: Kumar G. Belani, MBBS, MS.
Contribution: This author helped design the study, conduct the study, analyze the data, and write the manuscript.
Attestation: Kumar Belani has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.
Conflicts of Interest: Kumar G. Belani received honoraria from NONIN Inc., consulted for NONIN Inc., received research funding from NONIN Inc., received research funding from Augustine Temperature Management, LLC, reported a conflict of interest with Oakstone Publishing, consulted for Cadence Pharmaceuticals, and reported a conflict of interest with Cadence Pharmaceuticals. He is coordinating editor for Oakstone Publishing; he is a speaker for Cadence Pharmaceuticals. His authorship in this article will add to his academic productivity and may have an indirect influence on his compensation from University of Minnesota.
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Contribution: This author helped design the study, conduct the study, analyze the data, and write the manuscript.
Attestation: Mark Albrecht has seen the original study data, reviewed the analysis of the data, approved the final manuscript, and is the author responsible for archiving the study files.
Conflicts of Interest: Mark Albrecht received paid support (salary) from Augustine Temperature Management.
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Conflicts of Interest: The author has no conflicts of interests to declare.
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Conflicts of Interest: The author has no conflicts of interests to declare.

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Conflicts of Interest: Christopher Nachtsheim has received consulting fees from Augustine Temperature Management.
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REFERENCES

1. Lidwell OM. Clean air at operation and subsequent sepsis in the joint. Clin Orthop Relat Res 1986;211:91–102
2. Lidwell OM. Air, antibiotics and sepsis in replacement joints. J Hosp Infect 1988;11:18–40
3. Lidwell OM, Elson RA, Lowbury EJ, Whyte W, Blowers R, Stanley SJ, Lowe D. Ultraclean air and antibiotics for prevention of postoperative infection: a multicenter study of 8,052 joint replacement operations. Acta Orthop Scand 1987;58:4–13
4. Hooper GJ, Rothwell AG, Frampton C, Wyatt MC. Does the use of laminar flow and space suits reduce early deep infection after total hip and knee replacement? The ten-year results of the New Zealand joint registry. J Bone Joint Surg Br 2011;93:85–90
5. Miner AL, Losina E, Katz JN, Fossel AH, Platt R. Deep infection after total knee replacement: impact of laminar airflow systems and body exhaust suits in the modern operating room. Infect Control Hosp Epidemiol 2007;28:222–6
6. Brandt C, Hott U, Sohr D, Daschner F, Gastmeier P, Rüden H. Operating room ventilation with laminar airflow shows no protective effect on the surgical site infection rate in orthopedic and abdominal surgery. Ann Surg 2008;248:695–700
7. Harper CM, Andrzejowski JC, Alexander R. NICE and warm. Br J Anaesth 2008;101:293–5
8. Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. N Engl J Med 1996;334:1209–15
9. Dasari KB, Albrecht M, Harper M. Effect of forced air warming on operating theatre laminar flow ventilation performance. Anaesthesia 2012;67:244–9
10. Bräuer A, Quintel M. Forced-air warming: technology, physical background and practical aspects. Curr Opin Anaesthesiol 2009;22:769–74
11. Lenhardt R. Monitoring and thermal management. Best Pract Res Clin Anaesthesiol 2003;17:569–81
12. Bayazit Y, Sparrow EM. Energy efficiency comparison of forced-air versus resistance heating devices for perioperative hypothermia management. Energy 2010;35:1211–5
13. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for Prevention of Surgical Site Infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. Am J Infect Control 1999;27:97–132
14. Whyte W, Shaw BH. The effect of obstructions and thermals in laminar-flow systems. J Hyg (Lond) 1974;72:415–23
15. Jensen PA, Schafer MP. Sampling and characterization of bio-aerosols. Chapter J. In: NIOSH Manual of Analytical Methods. Cincinnati, Ohio: Department of Health and Human Services. 1998:82–112
16. Mackintosh CA, Lidwell OM, Towers AG, Marples RR. The dimensions of skin fragments dispersed into the air during activity. J Hyg (Lond) 1978;81:471–9
17. Brohus H, Balling KD, Jeppesen D. Influence of movements on contaminant transport in an operating room. Indoor Air 2006;16:356–72
18. McGovern PD, Albrecht M, Belani KG, Nachtsheim C, Partington PF, Carluke I, Reed MR. Forced-air warming and ultra-clean ventilation do not mix: an investigation of theatre ventilation, patient warming and joint replacement infection in orthopaedics. J Bone Joint Surg Br 2011;93:1537–44
19. Sessler DI, Olmsted RN, Kuelpmann R. Forced-air warming does not worsen air quality in laminar flow operating rooms. Anesth Analg 2011;113:1416–21
20. Deutsches Institut für Normung (DIN). Annex C: determining the degree of protection. Ventilation and air conditioning, Part 4. VAC systems in buildings and rooms used in the health care sector (DIN 1946-4:2008-12). 2008:1–67

EXHIBIT DX6

TO DECLARATION OF BENJAMIN W. HULSE IN SUPPORT OF DEFENDANTS' MOTION FOR RECONSIDERATION OF THE COURT'S DECEMBER 13, 2017 ORDER ON GENERAL CAUSATION

THE JOURNAL OF BONE & JOINT SURGERY

■ ARTHROPLASTY

Do forced air patient-warming devices disrupt unidirectional downward airflow?

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Patient warming significantly decreases the risk of surgical site infection. Recently there have been concerns that forced air warming may interfere with unidirectional airflow, potentially posing an increased risk of infection. Our null hypothesis was that forced air and radiant warming devices do not increase the temperature and the number of particles over the surgical site when compared with no warming device. A forced air warming device was compared with a radiant warming device and no warming device as a control. The temperature and number of particles were measured over the surgical site. The theatre was prepared as for a routine lower-limb arthroplasty operation, and the same volunteer was used throughout the study.

Forced air warming resulted in a significant mean increase in the temperature (1.1°C *vs* 0.4°C, $p < 0.0001$) and number of particles (1038.2 *vs* 274.8, $p = 0.0087$) over the surgical site when compared with radiant warming, which raises concern as bacteria are known to require particles for transport.

The rate of infection following joint replacement surgery of the lower limb is currently < 1%.[1] Both ultra-clean unidirectional airflow and patient warming contribute to reducing the risk of infection.[2-5] However, unidirectional downward airflow is vulnerable to external influences including lights, personnel and equipment. There are also concerns that forced-air warming devices disrupt unidirectional airflow, thus potentially causing a risk of infection.[6]

Ultra-clean unidirectional downward airflow was introduced by Charnley in the 1960s.[7] He reported a reduction in infection following total hip replacement (THR) from 9% to 1%.[7] There is a particular reduction in the rate of infection if it is combined with intravenous antibiotics and sterile occlusive theatre clothing.[8,9]

Whyte et al[2] investigated the use of unidirectional downward airflow and total body exhaust systems. They found that with only plenum ventilation and the use of conventional clothing, the mean airborne concentration of bacterial particles during a THR procedure was 450/m^3. Using unidirectional downward airflow, but still using conventional clothing, this count was reduced to 7.3/m^3, a 60-fold reduction.[2] However, when total body exhaust systems were used in conjunction with unidirectional airflow, the bacterial concentration was reduced even further to 0.63/m^3.[2]

In a multicentre study involving 8052 joint replacements, Lidwell et al[3] concluded that for operations performed within ultraclean air ventilation, the rate of bacterial contamination of the wound, deep joint sepsis, and major wound sepsis were substantially reduced when compared with those operations performed in conventionally ventilated rooms.

Vertical unidirectional airflow ventilation is more effective than horizontal ventilation, especially when combined with walls around the operating area reaching down to 30 cm from the floor, thus extending the unidirectional airflow.[2] Body-exhaust suits have also been shown to further reduce the number of airborne bacteria. Both of these systems are employed in our theatre set-up.

The MRC study in 1984[4] recommended using vertical unidirectional airflow and prophylactic antibiotics to reduce the rate of infection. It showed that the rate of infection fell from 3.4% to 1.7% with the use of ultra clean air alone; to 0.4% when ultra clean air was combined with antibiotics, and to 0.2% through the use of ultra clean air, antibiotics and occlusive clothing.[4]

Bacterial contamination of the air has been shown to be significantly reduced by using ultra clean unidirectional downward air.[2] Our theatre set-up attempts to extend the unidirectional downward airflow and create a barrier between sterile personnel and

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equipment and non-sterile personnel by the use of Howorth enclosure extensions (Howorth Air Technology, Bolton, United Kingdom). Chow and Yang[10] found that as long as unsterile personnel are kept at least one metre from the sterile area, the surgical sites were no cleaner than with conventional air.

In more recent years patient warming has been shown to reduce the risk of surgical site infections, cardiovascular events, peri-operative pain and bleeding by increasing blood flow and tissue oxygen tension in the operative site.[11-13] In addition, maintaining a patient's normothermic core body temperature has been found to decrease the duration of post-anaesthetic recovery and hospital stay.[11-13]

Mild peri-operative reduction in core body temperature is common during major surgery, and may promote wound infection by triggering thermoregulatory vasoconstriction and decreasing subcutaneous oxygen tension. Reduced levels of oxygen in tissue impairs oxidative killing by neutrophils and decreases the strength of the wound healing by reducing collagen deposition.[5] Reduced body temperature also directly impairs immune function, resulting in an increased risk of infection and a prolonged hospital stay.[5]

Kurz, Sessler and Lenhardt[5] undertook a double blinded randomised study into the effects of peri-operative hypothermia, and concluded that intra-operative core temperatures approximately 2°C below normal can triple the incidence of wound infection and prolong hospitalisation by about 20%.

For many years forced air warming has been shown to be an effective method in warming surgical patients undergoing arthroplasty. NICE guidelines state that it is required for patient warming.[14] There has been concern, however, that forced air warming could increase the risk of infection by disrupting unidirectional downward airflow. Also it has been shown that potentially pathogenic organisms can be detected in the hoses of warming devices;[15] however, no such organisms were detected by a study that placed microbial filters over the ends of the hoses.[16]

Sharp, Chesworth and Fern[17] investigated whether forced air warming increased the bacterial level in the operating field. They collected air samples with a slit air sampler, and found no colony forming units (CFUs) on any of the plates exposed inside the unidirectional downward airflow, although two samples taken at floor level had large numbers of CFUs.[17]

To date there have been no papers showing that forced air warming devices disrupt laminar airflow. This study aimed to test our null hypothesis that forced air and radiant warming devices do not increase the number of particles or affect the temperature at the site of the operation, when compared with no warming device.

Materials and Methods

Two devices were tested against a control (no warming device). The devices used were a torso forced air warming blanket (Bair Hugger; Arizant UK Limited, Wakefield, United Kingdom) and a radiant warming blanket (Hot-dog, Eden Prairie, Minnesota).

The operating theatre was set up for a routine lower-limb replacement operation in our unit (Northern General Hospital, Sheffield, United Kingdom). A volunteer, who was used throughout the study, was positioned supine on the operating table, without a tourniquet, and draped for a total knee replacement, within an ExFlow 90 Howorth enclosure with vertical wall extensions to 1 metre from the floor. The wall extensions aimed to maximise the unidirectional airflow below the operative site and also to prevent non-sterile theatre personnel from entering the enclosure. The surgeon wore sterile clothing, theatre hood and body exhaust hose. The simulated operation had a single surgeon with no theatre nurse, assistant, or trays within the enclosure and the lights were raised as high as possible, to minimise the disruption of airflow and to identify whether the number of particles or temperature over the surgical site was affected by either of the warming systems. The validation report on the ventilation system conformed to the requirements of the Health Technical Memorandum (HTM) 2025.[18]

Temperature measurements were taken before and 30 minutes after warming using a digital temperature probe positioned 10 cm above the surgical site, and outside the Howorth enclosure as a control to standardise the results. The increase in temperature was calculated by subtracting the temperature after 30 minutes from that before warming, and then standardised using the temperatures recorded during the same period outside the enclosure. This was repeated five times with each warming device (n = 5).

The number of particles was measured using a HandiLaz handheld counter (Particle Measuring Systems, Boulder, Colorado) positioned 10 cm over the surgical site, which measured three particle sizes; 0.3 μm, 0.5 μm and 5.0 μm. This was repeated five times. Particle entrainment was calculated as the mean number of particles of each size over the surgical site.

Statistical analysis. All the data was evaluated using two-tailed *t*-tests and p-values were considered to be statistically significant when less than 0.05.

Table I. Mean temperature difference over the surgical site with 95% confidence intervals

	Warming device		
	Forced air	Radiant	p-value*
Temperature difference (°C)	1.1 (1.05 to 1.15)	0.4 (0.37 to 0.43)	< 0.0001

* unpaired *t*-test

Results

The temperature over the surgical site increased significantly when the forced air warming device was used in comparison to the radiant warming device, or control (Table I).

Table II. Mean number of particles over the surgical site (CI, confidence interval)

	Mean number of particles (95% CI) [range]			
Particle size (μm)	Forced air	No warming	Radiant	p-value
0.3	1038.2 (973.1 to 1103.3) [965 to 1150]	274.8 (230 to 310) [193 to 308]	274.8 (231.5 to 318.1) [193 to 308]	0.0087
0.5	30.8 (28.7 to 32.9) [29 to 34]	5.8 (4.2 to 7.4) [4 to 8]	6.8 (5.2 to 8.4) [5 to 9]	0.0073
5.0	3.6 (2.9 to 4.3) [3 to 5]	0.8 (0.4 to 1.2) [0 to 1]	0.8 (0.4 to 1.2) [0 to 1]	0.0038

The number of particles over the surgical site was significantly higher when the force air warming device was used in comparison to the radiant warming device, or control (Table II).

Discussion

It is our view that both patient warming devices and unidirectional ultra clean downward airflow are needed in lower limb arthroplasty in order to reduce the risk of infection.

Because of the nature of our experiment we are unable to conclude that the use of the forced air warming device, which produced a change in temperature and an increase in the number of particles over the surgical site, would actually lead to an increased risk of surgical site infection. The results do suggest that the downward flow of air is disrupted, as the warming device was lower than at the surgical site.

Forced air warming significantly increased the number of airborne particles over the surgical site compared to the radiant warming or the control, both of which showed similar results. Bacteria require particles to transport them, and although we are unable to confirm if any of the particles were transporting bacteria, the significant increase in the number of particles that we found in this study at the surgical site is of concern.

We have shown that in our experimental theatre set-up forced air warming significantly increases the temperature and number of particles over the surgical site. This may occur via ingress of warm air from the warming device or by direct heating away from the patient, as the warming device creates multidirectional heating in comparison to the radiant warming device which creates unidirectional heating to the patient.

We are therefore able to reject our null hypothesis that forced air and radiant warming devices do not increase the temperature and the number of particles over the surgical site in comparison with no warming device.

Further work is required to confirm that unidirectional airflow is disrupted by forced air patient warming devices under our specific experimental theatre set-up and future studies are needed to visualise the airflow over the surgical site.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References

1. **Phillips JE, Crane TP, Noy M, Elliott TS, Grimer RJ.** The incidence of deep prosthetic infections in a specialist orthopaedic hospital: a 15-year prospective study. *J Bone Joint Surg [Br]* 2006;88-B:943–948.
2. **Whyte W, Lidwell OM, Lowbury EJ, Blowers R.** Suggested bacteriological standards for air in ultraclean operating rooms. *J Hosp Infect* 1983;4:133–139.
3. **Lidwell OM, Elson RA, Lowbury EJ, et al.** Ultraclean air and antibiotics for prevention of postoperative infection: a multicenter study of 8,052 joint replacement operations. *Acta Orthop Scand* 1987;58:4–13.
4. **Lidwell OM, Lowbury EJ, Whyte W, et al.** Infection and sepsis after operations for total hip or knee-joint replacement: influence of ultraclean air, prophylactic antibiotics and other factors. *J Hyg (Lond)* 1984;93:505–529.
5. **Kurz A, Sessler DI, Lenhardt R.** Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization: Study of Wound Infection and Temperature Group. *N Engl J Med* 1996;334:1209–1215.
6. **Tumia N, Ashcroft GP.** Convection warmers: a possible source of contamination in laminar airflow operating theatres? *J Hosp Infect* 2002;52:171–174.
7. **Charnley J.** Postoperative infection after total hip replacement with special reference to air contamination in the operating room. *Clin Orthop* 1972;87:167–187.
8. **Hauser R, Berchtold W, Schreiber A.** Incidence of deep sepsis in uncemented total hip arthroplasty using clean air facility as a function of antibiotic prophylaxis. *Bull Hosp Jt Dis* 1996;54:175–179.
9. **Lidwell OM.** Air, antibiotics and sepsis in replacement joints. *J Hosp Infect* 1988;11(Suppl C):18–40.
10. **Chow TT, Yang XY.** Ventilation performance in operating theatres against airborne infection: review of research activities and practical guidance. *J Hosp Infect* 2004;56:85–92.
11. **Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR.** Guideline for Prevention of Surgical Site Infection, 1999: Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. *Am J Infect Control* 1999;27:97–132.
12. **Mahoney CB, Odom J.** Maintaining intraoperative normothermia: a meta-analysis of outcomes with costs. *AANA J* 1999;67:155–163.
13. **Bayazit Y, Sparrow EM.** Energy efficiency comparison of forced-air versus resistance heating devices for perioperative hypothermia management. *Energy* 2010;35:1211–1215.
14. **No authors listed.** National Institute for Clinical Excellence: perioperative hypothermia (inadvertent), 2008 (NICE clinical guideline 65). http://www.nice.org.uk/nicemedia/pdf/CG65Publicinfo.pdf (date last accessed 26 September 2011).
15. **Albrecht M, Gauthier R, Leaper D.** Forced-air warming: a source of airborne contamination in the operating room? *Orthop Rev (Pavia)* 2009;1:e28.
16. **Avidan MS, Jones N, Ing R, et al.** Convection warmers: not just hot air. *Anaesthesia* 1997;52:1073–1076.
17. **Sharp RJ, Chesworth T, Fern ED.** Do warming blankets increase bacterial counts in the operating field in a laminar-flow theatre? *J Bone Joint Surg [Br]* 2002;84-B:486–488.
18. **No authors listed.** NHS Estates. Health Technical Memorandum 2025: ventilation in healthcare premises, 1998. http://www.mintie.com/assets/img/education/NHS%20Estates%20-%20HVAC.pdf (date last accessed 26 September 2011).

EXHIBIT DX7

TO DECLARATION OF BENJAMIN W. HULSE IN SUPPORT OF DEFENDANTS' MOTION FOR RECONSIDERATION OF THE COURT'S DECEMBER 13, 2017 ORDER ON GENERAL CAUSATION

THE BONE & JOINT JOURNAL

■ ARTHROPLASTY

Forced-air patient warming blankets disrupt unidirectional airflow

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We have recently shown that waste heat from forced-air warming blankets can increase the temperature and concentration of airborne particles over the surgical site. The mechanism for the increased concentration of particles and their site of origin remained unclear. We therefore attempted to visualise the airflow in theatre over a simulated total knee replacement using neutral-buoyancy helium bubbles. Particles were created using a Rocket PS23 smoke machine positioned below the operating table, a potential area of contamination. The same theatre set-up, warming devices and controls were used as in our previous study. This demonstrated that waste heat from the poorly insulated forced-air warming blanket increased the air temperature on the surgical side of the drape by > 5°C. This created convection currents that rose against the downward unidirectional airflow, causing turbulence over the patient. The convection currents increased the particle concentration 1000-fold (2 174 000 particles/m^3 for forced-air warming *vs* 1000 particles/m^3 for radiant warming and 2000 particles/m^3 for the control) by drawing potentially contaminated particles from below the operating table into the surgical site.

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Ultraclean unidirectional airflow has been shown to reduce significantly the risk of infection in lower limb joint replacement.[1-4] In recent years, patient warming has also been shown to afford significant benefit. Hypothermia causes peripheral vasoconstriction, which reduces the delivery of oxygen to soft tissues; this in turn impairs the oxidative killing of bacteria by neutrophils and lessens the strength of wound healing by reducing the deposition of collagen.[5] By increasing blood flow and the oxygen tension in the tissues, the risk of surgical site infection, cardiovascular events, peri-operative pain and bleeding is reduced.[6] In addition, the maintenance of a patient's normal core temperature reduces the duration of post-operative recovery and hospital stay.[5-8]

We reported with a particular arrangement in the operating theatre set-up, waste heat from forced-air warming can increase the particle concentration and temperature over the surgical site.[9] This implies that the downward unidirectional airflow is disrupted by the waste heat generated, although the mechanism of airflow disruption was unclear. The increased concentration of particles over the surgical site is of concern as it may transport bacteria. The purpose of this study was to visualise the airflow over the surgical site to see if the additional particles came from a potentially contaminated area.

Materials and Methods

We simulated the theatre set-up (Fig. 1) that we use for a total knee replacement at the Northern General Hospital (Sheffield, United Kingdom) with the exception that, in an attempt to isolate the effect of forced-air warming, there was only a single surgeon in the Howorth ExFlow 90 enclosure (Howorth Air Technology, Bolton, United Kingdom). A mannequin was placed supine on the operating table and a single knee replacement non-porous exclusion drape was hung vertically from the Howorth enclosure. The drape extended to the floor over the table and the opposite limb, so that only the knee being operated on was exposed. The enclosure walls extended down to within 1 m of the theatre floor. This created a confined area that extended the unidirectional airflow below the site of surgery and kept unscrubbed personnel out of the enclosure. The single surgeon wore a standard theatre gown, hood, mask and body exhaust hose that was attached outside the enclosure. Validation and verification checks of the ventilation system showed that it conformed to the requirements of the Health Technical Memorandum (HTM) 2025.[10]

We compared two warming devices and a control (no warming device). The two devices were a torso forced-air warming device (Bair Hugger; Arizant, Wakefield, United Kingdom)

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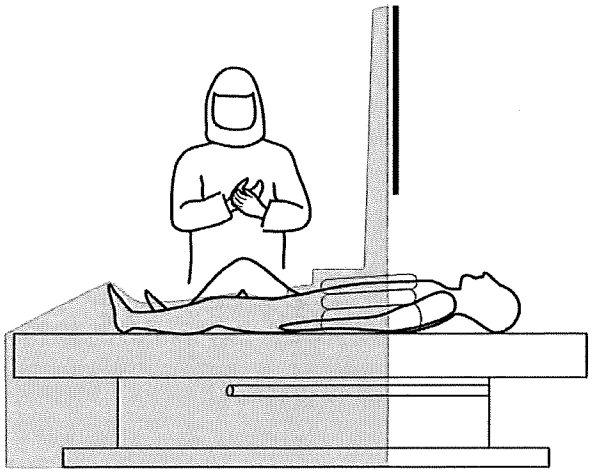

Fig. 1

Diagram showing the theatre set-up.

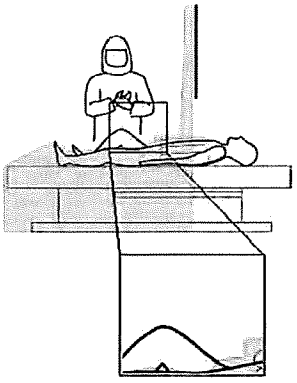

Fig. 2a

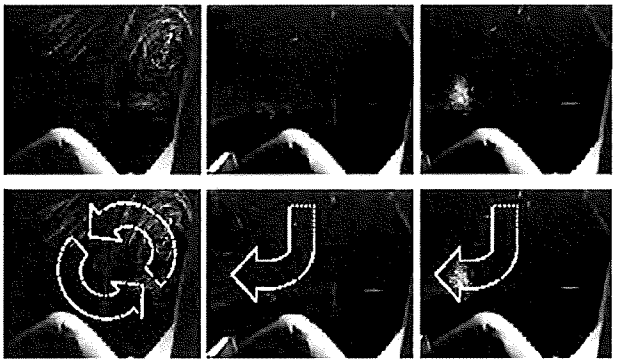

Fig. 2b

Figure 2a – diagram showing the area in which the airflow was assessed. Figures 2b – example photographs showing the visualisation of airflow using forced-air warming (left), radiant warming (centre) and none (right). The lower images are illustrated to emphasise the direction of airflow.

and a torso radiant warming device (HotDog, Eden Prairie, Minnesota). To see if particle entrainment occurred from a potentially contaminated area, a continuous flow of 0.3 µm glycerol tracer particles, created by a Rocket PS23 smoke machine (Pea Soup Ltd, Ingleby Barwick, United Kingdom), was introduced through a 1 m-long fenestrated tube secured below the table at the level of the surgeon's knees (Fig. 1). The smoke machine was connected to the fenestrated tube by a long hose to allow the particles to cool before entering the enclosure. All investigations were undertaken over one day, in a single theatre, with the same equipment and investigators.

Experimental design. The drape temperature, particle concentration and particle visualisation were each assessed five times for each warming device and control. The mean drape temperature and particle concentration were then calculated.

Airflow visualisation. The airflow was visualised using neutral-buoyancy helium soap bubbles, produced by a bubble generator (Sage Action, Ithaca, New York) and a high-intensity light source. The bubbles were produced using a mixture of helium, air, detergent, and a centripetal bubble size classification filter to produce neutrally buoyant bubbles of approximately 4 mm diameter. Photographs were taken using a digital camera (D300; Nikon, Melville, New York) with a shutter speed of 0.25 s to allow the path of the bubbles to be seen. Neutrally buoyant helium bubbles enable the easy visualisation of streamlines and pathlines in flow fields that are not easily seen using traditional methods.[11]

Particle sampling. The particle concentration over the surgical site was measured using a HandiLaz handheld particle counter (Particle Measuring Systems, Boulder, Colorado). This instrument has a sample volume of 0.084 m^3 and can measure particles of > 0.3 µm.

Drape temperature. The drape temperature was measured at the same point on each occasion in line with the exposed flexed knee using a digital temperature probe taped on to the exclusion drape on the left side of the surgeon. This was compared with the temperature of the theatre outside the Howorth enclosure, which was kept as stable as possible.

Statistical analysis. All data were evaluated using two-tailed *t*-tests. Statistical significance was assumed at p-values < 0.05.

Results

The theatre temperature remained stable throughout the entire investigation at 19.2°C (SD 0.36).

Airflow visualisation. Unidirectional airflow was significantly disrupted when forced-air warming was used. Convection currents were set up within seconds of the forced-air warming system starting up: the bubbles rose approximately 1 m above the operating site, moved away from the drape, and then fell directly on to the surgical site before rising again to start the next cycle (Fig. 2).

Table I. Particle entrainment concentration

Warming scenario	Concentration (particles/m^3)
Control	2000
Radiant warming	1000
Forced-air warming	2 174 000

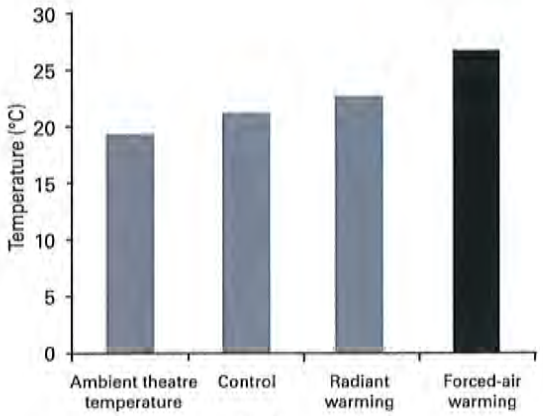

Fig. 3

Bar chart showing the theatre and drape temperatures for the various types of warming.

When the radiant warming device or the control was used there was no disruption of unidirectional airflow (Fig. 2). The bubbles moved away from the surgical site, then dispersed below the theatre table and out of the Howorth enclosure.

Particle entrainment. Forced-air warming significantly increased the concentration of particles over the surgical site (2 174 000 particles/m^3) compared with both the radiant warming device (1000 particles/m^3) ($p = 0.0002$) and the control (2000 particles/m^3) ($p = 0.0002$) (Table I). However, there was no significant difference between the radiant warming device and the control ($p = 0.1522$).

Vertical surgical drape temperature. Forced-air warming significantly increased the temperature of the drape compared with both the radiant warming device and the control, at increases of 4.3°C ($p = 0.0001$) and 5.4°C, respectively ($p = 0.0001$). However, there was no significant difference between the radiant warming device and the control (1.1°C; $p = 0.0539$) (Fig. 3).

Discussion

Unidirectional vertical airflow passes through high-efficiency particulate air (HEPA) filters, filtering particles of 0.3 µm with 99.97% efficiency to create a bacteria-free source of air.[12] The Howorth enclosure, when combined with vertical unidirectional airflow, aims to create within a designated space an entire body of air that has a uniform velocity and direction. It is designed to minimise the entrainment of particles, which are known to transport bacteria,[3] from outside the Howorth enclosure and from below the operating table. This is enhanced by the plenum effect of the pressure inside the theatre being greater than that outside, which creates exponential airflow and a net movement of air out of the theatre.

Unidirectional HEPA filtered airflow has been the standard requirement in joint replacement surgery for many years.[1-4] In addition, warming the patient with forced air has been shown to have significant benefits, including the reduction of surgical site infection, and forms part of the guidelines from the National Institute for Health and Clinical Excellence in the United Kingdom.[5-8,13] However, it had not previously been established whether warming the patient with forced air has any effect on unidirectional airflow.

In our experiment, the clearest interference with unidirectional airflow occurred when the mannequin was warmed with the forced-air device. Convection currents were established within a short period of time. Waste heat from the poorly insulated device warmed the drape and increased the air temperature over the surgical site. The warmed air rose against the downward unidirectional airflow, reaching a peak approximately 1 m above the surgical site at which point the air reached the cooler unidirectional airflow and then flowed back on to the operation site. This process was then repeated, creating convection currents. Once this cycle was established, particles were entrained in the airflow from below the table, drawn up into the vortex to fall on to the surgical site. Unidirectional airflow was not disrupted when either the radiant warming device or the control was used. There was little or no waste heat created from the radiant device, which was well insulated on the side not in contact with the patient.

It does not appear that the forced-air warming device itself blows potentially contaminated warm air directly into the Howorth enclosure. The device heats the drape covering it, leading to the creation of convection currents that meet the downward unidirectional airflow, causing turbulence.

We suggest that if the forced-air warming device was as well insulated on the surface that was not in contact with the patient as occurs with the radiant warming device, waste heat might not have warmed the vertical drape and created the convection currents.

If the theatre is set up as shown in Figure 1, waste heat significantly disrupts unidirectional airflow. Therefore, a warming device that disperses heat away from the patient should not be used. In other words, the surface not in contact with the patient needs to be well-insulated. If the theatre set-up uses Howorth wall extensions or a vertical drape between the surgical field and the anaesthetist, an enclosed environment is created. The potential benefits of this set-up are the exclusion of personnel from the interior of the enclosure. If the wall extensions and vertical drape that exclude the anaesthetist are not in place, the production of waste heat may not be as important because the air could leave the enclosure more easily.

The benefits of unidirectional airflow have been proven, as have the significant benefits of patient warming. Therefore it is important that both continue to be used. However, the set-up of the theatre and the effect of waste heat need to be taken into consideration, as they may have a detrimental effect on the unidirectional airflow and thus, potentially, the sterility of the surgical site.

This study does not show that forced-air warming increases the risk of infection – only that in certain types of theatre set-up it can significantly disrupt unidirectional airflow and draw particles from the potentially contaminated area below the sterile surgical field. This is a concern.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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References

1. **Charnley J.** Postoperative infection after total hip replacement with special reference to air contamination in the operating room. *Clin Orthop Relat Res* 1972;87:167–187.
2. **Hauser R, Berchtold W, Schreiber A.** Incidence of deep sepsis in uncemented total hip arthroplasty using clean air facility as a function of antibiotic prophylaxis. *Bull Hosp Jt Dis* 1996;54:175–179.
3. **Lidwell OM.** Air, antibiotics and sepsis in replacement joints. *J Hosp Infect* 1988;11(Suppl C):18–40.
4. **Lidwell OM, Lowbury EJ, Whyte W, et al.** Infection and sepsis after operations for total hip or knee-joint replacement: influence of ultraclean air, prophylactic antibiotics and other factors. *J Hyg (Lond)* 1984;93:505–529.
5. **Kurz A, Sessler DI, Lenhardt R.** Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization: Study of Wound Infection and Temperature Group. *N Engl J Med* 1996;334:1209–1215.
6. **Mahoney CB, Odom J.** Maintaining intraoperative normothermia: a meta-analysis of outcomes with costs. *AANA J* 1999;67:155–163.
7. **Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR.** Guideline for Prevention of Surgical Site Infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. *Am J Infect Control* 1999;27:97–132.
8. **Bayazit Y, Sparrow EM.** Energy efficiency comparison of forced-air versus resistance heating devices for perioperative hypothermia management. *Energy* 2010;35:1211–1215.
9. **Legg AJ, Cannon T, Hamer AJ.** Do forced air patient warming devices disrupt unidirectional downward airflow? *J Bone Joint Surg [Br]* 2012;94-B:254–256.
10. **No authors listed.** NHS Estates. Health Technical Memorandum 2025. Ventilation in Healthcare Premises. http://www.mintie.com/assets/img/education/NHS%20Estates%20-%20HVAC.pdf (date last accessed 15 November 2012).
11. **Kerho MF.** Neutrally buoyant bubbles used as flow tracers in air. *Experiments in Fluids* 1994;16:393–400.
12. **Thermo Electron Corporation.** Importance of Class 100 Air in a CO2 Incubator. http://www.ninolab.se/fileadmin/Ninolab/pdf/thermoforma/Class100_white_paper_11663.pdf (date last accessed 7 January 2013).
13. **No authors listed.** National Institute for Clinical Excellence. Management of inadvertent perioperative hypothermia in adults: NICE clinical guideline 65, 2008. http://www.nice.org.uk/CG065 (date last accessed 14 November 2012).

EXHIBIT DX8

TO DECLARATION OF BENJAMIN W. HULSE IN SUPPORT OF DEFENDANTS' MOTION FOR RECONSIDERATION OF THE COURT'S DECEMBER 13, 2017 ORDER ON GENERAL CAUSATION

Anaesthesia 2012, 67, 244–249 doi:10.1111/j.1365-2044.2011.06983.x

Original Article

Effect of forced-air warming on the performance of operating theatre laminar flow ventilation*

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Summary

Forced-air warming exhaust may disrupt operating theatre airflows via formation of convection currents, which depends upon differences in exhaust and operating room air temperatures. We investigated whether the floor-to-ceiling temperatures around a draped manikin in a laminar-flow theatre differed when using three types of warming devices: a forced-air warming blanket (Bair Hugger™); an over-body conductive blanket (Hot Dog™); and an under-body resistive mattress (Inditherm™). With forced-air warming, mean (SD) temperatures were significantly elevated over the surgical site vs those measured with the conductive blanket (+2.73 (0.7) °C; $p < 0.001$) or resistive mattress (+3.63 (0.7) °C; $p < 0.001$). Air temperature differences were insignificant between devices at floor ($p = 0.339$), knee ($p = 0.799$) and head height levels ($p = 0.573$). We conclude that forced-air warming generates convection current activity in the vicinity of the surgical site. The clinical concern is that these currents may disrupt ventilation airflows intended to clear airborne contaminants from the surgical site.

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Patient warming systems are widely used to prevent unintentional peri-operative hypothermia based on the established benefits of reduced blood loss and transfusion [1], improved wound healing [2], reduced duration of hospital stay [3], improved survival [4] and reduced surgical site infection rates [5]. However, patient warming systems also release excess heat into the operating theatre that may generate convection currents even within a laminar flow system. It is possible that convection currents could disrupt the intended ceiling-to-floor theatre airflows and therefore impede the ventilation system's ability to clear contaminants from the surgical site.

There are two distinct categories of patient warming technology, forced-air and conductive heating. Forced-air devices deliver a heated airflow to a disposable coverlet that vents the hot air over the patient's body [6]. Conductive heating devices employ an electrically heated pad in contact with the patient's body [7]. Both types of devices appear to be comparably effective for the prevention of accidental peri-operative hypothermia [8–14], although forced-air devices are less efficient in transferring the applied heat to the patient than conductive devices [15]. Therefore, we might expect forced-air devices to generate a greater excess heat load on the ventilation system.

When considered in combination with other established sources of ventilation disruption such as surgical lights and personnel [16], even moderate changes in the excess heat load are of clinical importance. For example, convection currents due to forced-air warming occur in the vicinity of the surgical site. They are formed in the downstream 'wake' created by overhead lights and regions of blocked ventilation flow created by drapes and/or personnel. Convection currents were not observed when conductive patient warming devices were used [17]. McGovern et al. postulated that the observed disruption was due to excess heat as the result of patient warming excess heat, yet they made no measurements of ventilation field temperature nor did they establish the 'thermal' basis of such disruption.

Conceptually, the thermal basis of laminar flow disruption is the opposition of downward ventilation air currents by buoyancy-driven hot air convection currents. We assessed ventilation performance by measuring changes in ventilation field temperatures using a forced-air blanket (Bair Hugger™ 525; Arizant Healthcare Inc., Eden Prairie, MN, USA), with an over-body conductive blanket (Hot Dog™ B103; Augustine Temperature Management, Eden Prairie, MN, USA) and an under-body resistive mattress (Inditherm™ OTM1, Rotherham, UK) as controls. Our (null) hypothesis was that the use of forced-air warming would result in ventilation field temperatures similar to the conductive patient warming devices.

Methods

Experiments were conducted in a partial-walled ultraclean operating theatre (ExFlow 90, Howorth, UK; Validation certification QA ref AA719/1/SM) used for orthopaedic surgery (Royal Sussex County Hospital, UK). A manikin was placed in the supine position and a general surgical drape applied with the head end tented to form an anaesthesia screen (Fig. 1). The foot end of the drape was raised and folded over to create an air channel that directed the forced-air warming exhaust out of the ventilation field. A lower-body patient warming device (either the Bair Hugger, Hot Dog or Inditherm) was introduced under the drape (Fig. 2).

Ventilation field temperatures (Fig. 1) were measured floor-to-ceiling using 24 thermistors (KIMO KH200 Temperature and Humidity Loggers; Kimo, Montopon, France) placed across five heights:- floor (~5 cm above the floor); table (on the drape, ~60 cm from the floor); patient (2 cm above the dummy, ~80 cm from the floor); head (25 cm above the dummy, ~105 cm from the floor); ceiling (high level in the laminar flow, ~210 cm from the floor); and five locations (left shoulder, right shoulder, surgical site (abdomen), left knee, right knee); 24 locations resulted instead of 25 as it was not possible to measure the surgical site location at table height.

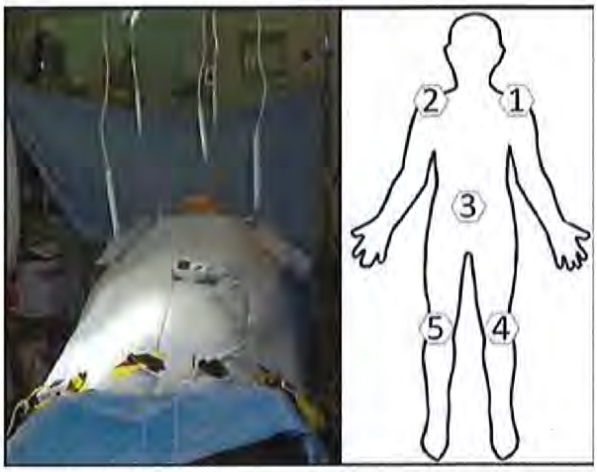

Figure 1 Manikin with raised foot drape and thermistors placed at 5 heights (floor, table, patient, head, overhead supply plenum) across five locations shown as (1) left shoulder; (2) right shoulder; (3) surgical site (abdomen); (4) left knee; and (5) right knee.

With each of the three patient warming devices, ventilation field temperatures were recorded at 60-s intervals for: (1) a 20-min 'control' period with the patient warming device turned off; (2) a 'transition' period of ~10 min when the patient warming device was turned on but had not thermally equilibrated with the ventilation environment; and (3) a 20-min 'steady-state' period when the patient warming device had thermally equilibrated and ventilation field temperatures had stabilised.

Air temperature differences from the overhead supply were computed by subtracting the time series of ventilation field temperatures at each location and height from the corresponding time series obtained at ceiling height for that location. Increases in air temperature were assessed as the average of this differenced time series for each location, height, time period

Figure 2 Patient warming devices evaluated: (a) under-body resistive mattress (Inditherm); (b) over-body conductive fabric blanket (Hot Dog); and (c) forced-air blanket (Bair Hugger).

(i.e. control, transition, steady state) and patient warming device.

Two separate classes of ANOVA models were fitted to the data. The first class assessed whether increases in air temperature were significantly different between patient warming devices when compared across control and steady-state periods for a given height. Formally, this difference between patient warming devices was assessed via the interaction term of an ANOVA model having 'increase in air temperature' as the response and 'blocking effects of period' (two levels: control and steady state) and 'environment' (three levels: forced-air warming run, conductive fabric run, and resistive mattress run) as the factors. Inclusion of a separate 'warming device' main effect in the model was not possible because it is perfectly correlated with the 'environment blocking term'. In other words, the main effect of warming device cannot be distinguished from, say, a 2 °C increase in overall environmental theatre temperature due to the time of day. Furthermore, we were interested in temperature increases by warming device for the steady-state period vs control period (which is the effect measured by the interaction term). The p value of interest is therefore the significance of the model interaction term when compared with an additive model using a log-likelihood ratio test.

A second class of ANOVA model was fitted to the temperature data for heights having a significant interaction term as described in the first model class. The purpose of this second model was to assess increase in air temperature vs control by location for a given height. Formally, an ANOVA model with interactions was fitted to the data for each significant height having increase in air temperature as the response and the following predictors: (1) 'environment blocking term' (three levels: forced-air run, conductive fabric run, and resistive mattress run); (2) 'location' (three levels: shoulder, surgical site which was always the abdomen, and knee); and (3) 'period' (two levels: control and steady state). It was necessary to pool the right and left measurements at the knee and shoulder locations to form replicates for inference. Means and standard errors are the maximum likelihood parameter estimates and p values were computed by applying t-tests to model parameter contrasts.

Results

Figure 3 shows an example of the temperature recordings obtained over the course of an experiment, with control, transition and steady-state periods highlighted.

The measured increase in air temperature vs control for each device by location and height (Fig. 4) showed forced-air warming to result in the greatest temperature increase at the patient height locations; for locations at the other heights (floor, table, head), there appeared to be no significant differences in air temperature between warming devices. This was confirmed by ANOVA; increases in steady-state air temperature vs control were significantly different between warming devices at the patient height ($p = 0.012$), but not at the other heights of floor ($p = 0.339$), table ($p = 0.799$) and head ($p = 0.573$).

A second class of ANOVA models was fitted to the patient height data to determine the specific effects of

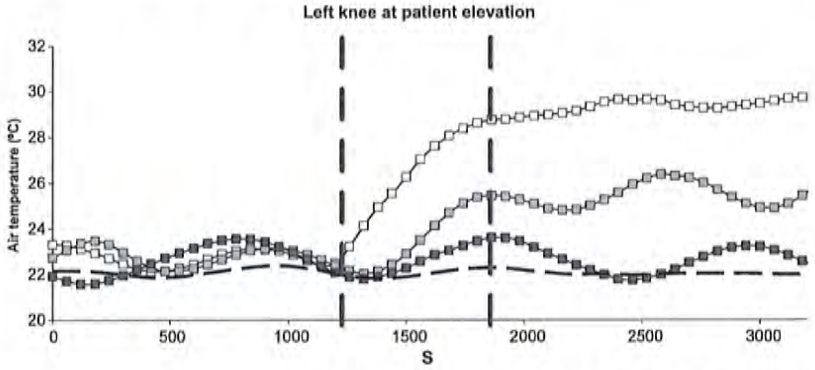

Figure 3 Absolute air temperature measurements for a single location (1 of 24) showing control period with patient warming device off (time = 0 to ~1200 s); transition period after turning device on (time = ~1200 s to ~1700 s) and steady state (from time = ~1700 s). Note the slightly varying temperature from the overhead supply. Temperature differences from the overhead supply were computed for the steady-state data and analysed for device comparisons. (-■-) resistive mattress, (-▭-) conductive blanket, (-□-) forced-air, (—) average overhead supply.

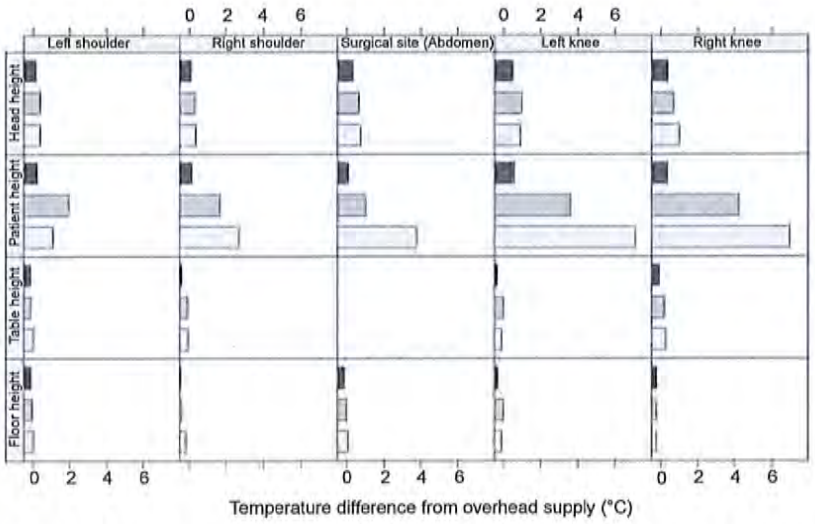

Figure 4 Steady-state increase in air temperature from the overhead supply for each patient warming device by location and elevation. (■) resistive mattress, (▭) conductive blanket, (□) forced-air

each patient warming device by location; these models were not applied to the floor, table, and head height data as there were no significant temperature differences vs control. There were significant differences in mean (SD) patient height air temperature vs control between warming devices at the locations of: knee, with forced-air 3.2 (0.5) °C ($p < 0.001$) higher than conductive fabric and 6.6 (0.5) °C ($p < 0.001$) higher than the resistive mattress; surgical site, with forced-air 2.7 (0.7) °C ($p < 0.001$) higher than conductive fabric and 3.6 (0.7) °C ($p < 0.001$) higher than the resistive mattress; and shoulder, with forced-air 1.7 (0.5) °C ($p = 0.01$) higher than resistive mattress. Differences were not significant between forced-air and conductive fabric at the shoulder location. Furthermore, conductive fabric air temperatures were significantly higher than the resistive mattress by 1.6 (0.5) °C ($p = 0.001$) and 3.5 (0.5) °C ($p < 0.001$) for the locations of shoulder and knee, respectively; these differences were not significant at the surgical site.

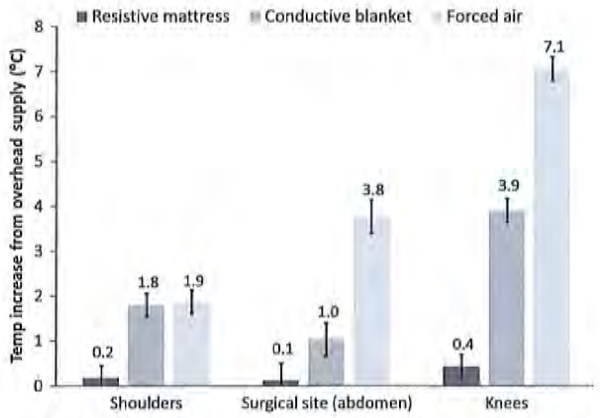

Figure 5 Average temperature increase from overhead supply at patient height by location. Right and left measurements for the shoulder and knee were pooled to allow for an estimate of dispersion. Error bars are SD.

Discussion

Our result rejects the null hypothesis, as we found forced-air warming to generate increased ventilation field temperatures vs both conductive warming devices. This finding suggests that forced-air warming technologies release significantly higher levels of excess heat than conductive warming technologies. Furthermore, forced-air warming temperature elevations were found to be the greatest above and around the surgical site. This finding is of concern because temperature elevations are the direct result of hot air-pockets moving upwards and against the downward laminar airflow currents. We can surmise this because air has a high transmissivity (i.e. low infrared absorption) [18]; thus, any temperature elevations are the result of convection current activity.

McGovern et al. used neutrally buoyant detergent bubbles released into theatre and found that forced-air warming appears to have a profound impact on laminar ventilation air-flows: there was large-scale dispersion of bubbles from the floor to the ceiling [17]. Our findings differ, in that we observed convection current activity directly above the patient and minimal activity elsewhere with forced-air warming. These differences could be due to the arrangement of the drapes; in our study, we raised the foot end of the drape to channel the forced-air warming exhaust outside the ventilation environment, whereas this channel was not present in the study of McGovern et al. in which the foot end of the drape extended to the floor. Therefore, the mass-flow of forced-air exhaust appears to play a critical role in the degree of ventilation disruption. Further studies are warranted to investigate whether specialised draping arrangements can lessen the risks of convection current formation. Both studies, however, confirmed that conductive warming technologies have little or no impact on ventilation airflows.

Although we attempted to mimic real conditions to a certain extent by having two people walk around within the laminar flow area, in a working operating theatre there are more people and many other ways by which the system might be disrupted [16, 17]. Another limitation of our study is that the definitive effects of this excess heat on clinical outcomes are presently unknown. Any future study might focus on particular types of surgery (e.g. that for device or joint implantation) where even small increases in airborne contamination are likely to be of more relevance [19]. Our findings may in part explain some aspects of the results of national studies over past 10 years, in which laminar flow ventilation has demonstrated either similar [20] or even higher [21, 22] infection rates than its conventional counterpart.

Balanced against these considerations, the prevention of hypothermia reduces the incidence of adverse events. Forced-air warming has been used on millions of patients and has been shown to be effective for managing unintended peri-operative hypothermia. The choice of warming device depends on a number of factors including the evidence base for the technology, cost, noise and even complaints from surgeons that they themselves become too warm [23]. Disruption of laminar flow should be one further objective factor guiding the proper choice.

Competing interests

Augustine Temperature Management loaned the Hot Dog conductive blanket and paid for the costs of temperature mapping. MA received paid support from Augustine Temperature Management for statistical analysis and manuscript preparation. No other external funding or competing interests declared.

References

1. Schmied H, Kurz A, Sessler DI, Kozek S, Reiter A. Mild hypothermia increases blood loss and transfusion requirements during total hip arthroplasty. *Lancet* 1996; **347**: 289–92.

2. MacFie CC, Melling AC, Leaper DJ. Effects of warming on healing. *Journal of Wound Care* 2005; **14**: 133–6.
3. Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. *New England Journal of Medicine* 1996; **334**: 1209–15.
4. Mahoney CB, Odom J. Maintaining intraoperative normothermia: a meta-analysis of outcomes with costs. *AANA Journal* 1999; **2**: 155–63.
5. Kumar S, Wong PF, Melling AC, Leaper DJ. Effects of perioperative hypothermia and warming in surgical practice. *International Wound Journal* 2005; **3**: 193–204.
6. Bräuer A, Quintel M. Forced-air warming: technology, physical background and practical aspects. *Current Opinion in Anesthesiology* 2009; **6**: 769–74.
7. Lenhardt R. Monitoring and thermal management. *Best Practice and Research: Clinical Anaesthesiology* 2003; **4**: 569–81.
8. Wong PG, Kumar S, Leaper DJ. Systemic warming as an adjunct to resuscitation in peritonitis: a pilot, randomized controlled trial. *Surgical Infections* 2007; **8**: 387–95.
9. Wong PF, Kumar S, Bohra A, Whetter D, Leaper DJ. Randomized clinical trial of perioperative systemic warming in major elective abdominal surgery. *British Journal of Surgery* 2007; **94**: 421–6.
10. Ng V, Lai A, Ho V. Comparison of forced-air warming and electric heating pad for maintenance of body temperature during total knee replacement. *Anaesthesia* 2006; **61**: 1100–4.
11. Janke EL, Pilkington SN, Smith DC. Evaluation of two warming systems after cardiopulmonary bypass. *British Journal of Anaesthesia* 1996; **77**: 268–70.
12. Kimberger O, Held C, Stadelmann K, et al. Resistive polymer versus forced-air warming: comparable heat transfer and core rewarming rates in volunteers. *Anesthesia and Analgesia* 2008; **107**: 1621–6.
13. Negishi C, Hasegawa K, Mukai S, Nakagawa F, Ozaki M, Sessler DI. Resistive-heating and forced-air warming are comparably effective. *Anesthesia and Analgesia* 2003; **96**: 1683–7.
14. Matsuzaki Y, Matsukawa T, Ohki K, Yamamoto Y, Nakamura M, Oshibuchi T. Warming by resistive heating maintains perioperative normothermia as well as forced-air heating. *British Journal of Anaesthesia* 2003; **90**: 689–91.
15. Bayazit Y, Sparrow EM. Energy efficiency comparison of forced-air versus resistance heating devices for perioperative hypothermia management. *Energy* 2010; **35**: 1211–5.
16. Whyte W, Shaw BH. The effect of obstructions and thermals in laminar-flow systems. *Journal of Hygiene (London)* 1974; **72**: 415–23.
17. McGovern PD, Albrecht M, G Bellani K, et al. Forced-air warming and ultra-clean ventilation do not mix: an investigation of ventilation disruption and joint sepsis in orthopaedics. *Journal of Bone and Joint Surgery, British Volume* 2011; **93-B**: 1537–44.
18. Incropera FP, DeWitt DP. *Introduction to Heat Transfer*, 4th edn. New York, NY: Wiley, 2001.
19. Petty W, Spanier S, Shuster JJ, Silverthorne C. The influence of skeletal implants on incidence of infection. Experiments in a canine model. *Journal of Bone and Joint Surgery, American Volume* 1985; **67**: 1236–44.
20. Miner AL, Losina E, Katz JN, Fossel AH, Platt R. Deep infection after total knee replacement: impact of laminar airflow systems and body exhaust suits in the modern operating room. *Infection Control and Hospital Epidemiology* 2007; **28**: 222–6.
21. Hooper GJ, Rothwell AG, Frampton C, Wyatt MC. Does the use of laminar flow and space suits reduce early deep infection after total hip and knee replacement?: The ten-year results of the New Zealand Joint Registry. *Journal of Bone Joint Surgery (British Volume)* 2011; **93**: 85–90.
22. Brandt C, Hott U, Sohr D, Daschner F, Gastmeier P, Rüden H. Operating room ventilation with laminar airflow shows no protective effect on the surgical site infection rate in orthopedic and abdominal surgery. *Annals of Surgery* 2008; **248**: 695–700.
23. Weirich TL. Hypothermia/warming protocols: why are they not widely used in the OR? *AORN Journal* 2008; **87**: 333–44.

EXHIBIT DX9

TO DECLARATION OF BENJAMIN W. HULSE IN SUPPORT OF DEFENDANTS' MOTION FOR RECONSIDERATION OF THE COURT'S DECEMBER 13, 2017 ORDER ON GENERAL CAUSATION

UNITED STATES DISTRICT COURT

DISTRICT OF MINNESOTA

In re Bair Hugger Forced Air Warming Products Liability Litigation,	)	MDL No. 15-2666 (JNE/FLN)
	)	VOLUME II
	)	PAGES 211-324

VIDEOTAPED DEPOSITION OF JONATHAN SAMET, M.D.

LOS ANGELES, CALIFORNIA

TUESDAY, AUGUST 8, 2017

JOB NO. 128394

DORIEN SAITO, CSR 12568, CLR

Ridgeview and do -- and following the protocol by using 2007 and comparing it to 2008 and 2009, Dr. Augustine picked out the data only for knees, used 2006, ignored 2007, and then used 2008 and '9, and entered those into the -- the calculus for the multicenter pooled results.

Would you agree with me that that would be a -- an improper methodological approach to presenting data?

MS. CONLIN: The same objection.

THE WITNESS: Well, again, under the assumptions you've given, it would suggest that he did not follow his protocol as described, albeit briefly, in the materials and methods.

BY MR. GORDON:

Q And throughout your career, you've been troubled by the misuse of data and science by the tobacco industry, haven't you?

A At times, yes.

Q Yeah.

Well, have there any times you've been -- you haven't been troubled by the misuse --

A Well --

Q -- of the science by the tobacco --

A -- I -- I think perhaps I was referring to science in those matters and the like, yes.

Q Any day with a y in it, basically; right?

If -- if what I'm telling you is true, if the -- if the evidence I'm providing you is true that the -- the owner of the company that is competing, is trying to sell a competitive product to forced-air warming is using data in the way I've -- I've described it to you, does -- does that give you any kind of similar concerns about the way -- similar to the way the tobacco industry manipulated and misused data?

A Well, I -- I would simply say that, you know, under the assumptions that you have listed, again if Augustine deviated from the protocol and perhaps to have a high odds ratio in the Center Number 1, that would certainly represent a deviation from appropriate scientific practice.

Q Would that bother you?

A If that were the case, it would bother me, yes.

MR. GORDON: Could we take a quick break?

THE WITNESS: Yeah. Absolutely. So why don't we -- how --

THE VIDEOGRAPHER: The time is 9:58 a.m. We are off the record.

(A brief recess was taken.)

THE VIDEOGRAPHER: We are back on the

record. The time is 10:07 a.m.

BY MR. GORDON:

Q Dr. Samet, if you were to disregard the McGovern -- the observational component of the McGovern paper and disregard the Augustine paper, just assume for the purposes of my question those two things either did not exist or you concluded for whatever reason that they're just -- they're just not reliable, would you still be of the opinion that the Bair Hugger is a substantial contributing cause to deep joint infections?

A Well, I mean, I think in my expert report, I lay out the mechanistic basis for the plausibility of the association that is observed in -- particularly in the McGovern paper at the time of my expert report.

The McGovern paper supplies the only estimate of the risk associated for deep joint infection associated with use of the forced-air warming Bair Hugger device. So absent the quantitative estimate from that paper, it would be -- while there would be a quite plausible mechanistic basis for increased risk, there would not been asked an association in -- in the real world.

Q So without McGovern and without the -- excuse me. I want to be clear. I'm not talking about the

bubble component of McGovern. I'm talking about only the observational component and now the Augustine.

Without those two things, would you agree that you could -- would no longer be in a position to opine that the Bair Hugger was a substantial contributing cause -- factor causing joint infections?

A Well, again, the basis on which the --

(Mr. Boone joins the deposition proceeding.)

THE WITNESS: -- magnitude of the association was considered in my report comes from the McGovern estimate. And absent that estimate, I would not have another way to construct a quantitative estimate.

BY MR. GORDON:

Q And without a way to construct a quantitative estimate, you couldn't say whether something was or was not a substantial contributing cause; right?

A I would not be able to judge the quantitative magnitude of the association.

Q In fact, based on the -- what you describe as the mechanistic basis -- information -- mechanistic data, all that does is -- is lead to a possibility, not a probability; right?

A Well, again, I think -- I wouldn't use the

EXHIBIT DX10

TO DECLARATION OF BENJAMIN W. HULSE IN SUPPORT OF DEFENDANTS' MOTION FOR RECONSIDERATION OF THE COURT'S DECEMBER 13, 2017 ORDER ON GENERAL CAUSATION

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Methicillin sensitive staphylococcus aureus screening and decolonisation in elective hip and knee arthroplasty

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SUMMARY

Aims: Periprosthetic joint infection (PJI) is a catastrophic and potentially life threatening complication following arthroplasty. In addition to the resulting impact on patient morbidity and mortality, PJI is associated with significant financial cost, which is estimated at £21,937 per case. Methicillin sensitive staphylococcus aureus (MSSA) is a common isolate in PJI and colonisation is a proven risk factor for subsequent infection. The aims of this study were: (1) to determine if MSSA screening and decolonisation reduced MSSA PJI rate in primary joint replacement and (2) to determine cost effectiveness of such a screening program.

Methods: Pre-operative screening for MSSA was introduced in our institution in 2010. All MSSA positive patients attending for elective arthroplasty were prescribed Octenisan body wash and nasal Bactroban for use 5 days prior to procedure, and five days after. Infection data was collected prospectively and compared with a control group from before.

Results: Between 2007 and 2014, 12,910 primary arthroplasties (5917 hip, 6993 knee) were performed. There were 3593 in the pre-screening group and 9318 in the post-screening group. Pre-screening PJI MSSA rate was 0.75% which reduced to 0.25% post screening introduction ($p < 0.0001$). Overall PJI rate fell from 1.92% to 1.41% ($p = 0.03$). The screening program was most effective in MSSA prevention in total hip arthroplasty (3% to 1.5%, $p = 0.002$) and significant in the multivariate analysis. Following the introduction of the screening programme 47 PJIs were avoided, with a cost per infection prevented of £1893.

Conclusion: The MSSA screening and eradication protocol used in our institution was effective at reducing rates of MSSA PJI. Furthermore, it resulted in significant savings when compared to the cost of prevented infections.

Introduction

The number of joint replacements performed is increasing year on year with an aging population.[1,2] This is in addition to hemiarthroplasty implants used for treating elderly patients with a hip fracture. Periprosthetic joint infection (PJI) is a serious and potentially life threatening complication.[3] According to the 12th annual national joint registry (NJR) report[4] the revision burden for infection stands at 1332 (14% of total revisions) per annum for Hip arthroplasty and 1417 (23%) for Knee arthroplasty. A large proportion of patients have debridement and retention of a prosthesis; that is not included in the NJR and therefore the true implication of PJI on the health service is much worse. This burden is increasing and similar across different health care systems.[5] With revision surgery having higher morbidity and mortality than a primary procedure every effort should be made to minimize PJI.[6] There is also a cost burden associated with treatment of infection and this can be anywhere between £15,000– £20,000, with costs escalating for revision procedure and recently estimated to be as much as £21,937 per revision in British practice.[7–9] The solution is almost always further aggressive surgery or lengthy courses of antibiotics to suppress the infection, or both. Despite current treatments, the relative survival rate of patients with PJI is 87.3% at five years. For comparison, the five-year relative survival rates for the top five most common cancers are 99% for prostate cancer, 89% for breast cancer, 17% for lung and bronchial cancer, 65% for colorectal cancer, and 92% for melanoma.[10]

Staphylococcus species are a common isolate in PJI[11] with Methicillin Sensitive Staphylococcus Aureus (MSSA) being the predominant pathogen isolated in 24.6% and Methicillin Resistant Staphylococcus Aureus (MRSA) 3.3% in England.[12] Between 25–30% of the United Kingdom population is positive for skin or nasal carriage of Staphylococcus, with MSSA prevalence estimated

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Table 1
Demographics and risk factors.

	2007–2009 ($n=3593$)	2010–2014 ($n=9318$)	p value
Gender % (M:F)	**46/54**	**45/55**	**0.1**
Mean age (range)	68.5 (22–100)	68.6 (16–99)	0.571
Mean BMI (range)	**29.5 (17.3–50.2)**	**29.9 (15.6–61)**	**0.009**
Mean length of stay (range)	5.61 (0–59)	3.85 (0–64)	<0.0001

at 20%.[13–15] Colonisation is a proven risk factor for subsequently developing surgical site infection during hospital stay with isolates matching those of nasal swabs in 85% of cases, suggesting that the majority of PJI are endogenous.[16–18] Decolonisation would therefore be expected to have a positive impact in reducing PJI. MRSA screening and decolonisation is well attested in the literature to be effective at reducing infection rates.[14,15,17] Evidence is emerging that screening programme for MRSA and MSSA may lead to a reduction in Staphylococcus infection rate.[19] In a double blind placebo controlled multi center trial of surgical patients decolonised with mupirocin and chlorhexidine verses placebo, the rate of MSSA SSI was lower in the treatment group (3.4% v 7.7%, relative risk of infection 0.42), although total SSIs were not reported.[20] Other studies have shown that mupirocin is effective at reducing nasal colonisation and that cost saving can be made by screening.[20–22]

The study aims to determine if MSSA screening and decolonisation programme can reduced MSSA PJI rates in primary joint replacement. A secondary aim is to determine cost effectiveness of such screening programme.

Methods

In 2010 our institution adopted a pre operative screening and decolonisation programme for carriers of MSSA in elective joint replacement along with standard mandatory MRSA screening. Prior to the introduction of screening there was no set protocol for MSSA screening and eradication, while MRSA testing and decolonisation was performed across the whole study period. The screening programme consists of swab collection for MRSA and MSSA. Nasal and groin swabs are taken at pre operative screening by a trained practitioner and the method of collection and site (nose and groin) did not vary between the pre and post MSSA screening groups. The swabs were processed in the microbiology laboratory on Colorex *Staphylococcus aureus* media (E & O Laboratories Ltd, England) plates were read between 18 and 24 h pink colonies went on for further identification using the VITEK MS (MALDI –TOF, Biomerieux, France) and sensitivity testing using the VITEK 2 (Biomerieux, France). The clinical team was alerted to all positive swabs. All patients attending for elective arthroplasty are given Octenisan bodywash (Octenidin, Schülke & Mayr UK Ltd, Sheffield, UK) to use for 5 days prior to surgery. Those found to be MSSA positive are additionally given Bactroban (Mupirocin, GlaxoSmithKline UK Limited, Brentford, UK) to be applied to both nostrils four times per day for 5 days prior to the procedure and for 5 days after. No further swabs were taken to confirm eradication on admission.

Northumbria Healthcare NHS Foundation Trust performs arthroplasty surgery in three hospitals with the surgical team operating across the different locations. The make up of the surgical team and implants used did not significantly change throughout the study period. A single infection surveillance team monitors infection rates for all cases and gathers data centrally. Data from Public Health England surgical site infection surveillance service was crossed referenced with this centrally gathered data. Public Health England's published standard on superficial, deep and organ space infection identified those hip and knee arthroplasties that had been complicated by PJI.[23] The use of this standard remained constant during the study period. Data obtained for procedure performed, age, gender, body mass index (BMI), American society of anaesthesiologist (ASA) physical status, duration of surgery, length of hospital stay (LOS), causative organism and sensitivities. Infection monitoring has been performed with complete data available from prior to screening programme (1st January 2007 to 31st December 2009) and after its introduction (1st January 2010 to 31st August 2014). This study is a retrospective review of this prospectively collected data.

Table 2
Pre and post screening ASA grade.

ASA	2007–2009 (n)	%	2010–2014 (n)	%
1	**332**	**12.3**	**1193**	**13.2**
2	1933	71.3	6549	72.3
3	**437**	**16.1**	**1269**	**14.0**
4	8	0.3	42	0.5

Statistical analysis was performed using STATA (StataCorp. 2013. *Stata Statistical Software: Release 13*. College Station, TX: StataCorp LP) all results quoted to three significant figures. Categorical data was analysis using $\chi 2$ test, continuous by an independent samples T-test. Significant variables were then used to build a logistic regression model. For those PJI with multiple organisms, if any of the cultured organisms included MSSA then they were included in the MSSA group for analysis.

Results

There were 12,911 hip and knee arthroplasties performed during the study period, with 3593 in the pre-screening group and 9318 in the post-screening group.

Demographics

Details of demographics and risk factors for PJI are presented in Tables 1 and 2. The duration of length of stay decreased significantly after 2010. The BMI was slightly higher in the study group (t-test, $p=0.009$) and also the ASA status of the two groups was significantly different (Chi squared $p=0.02$).

Infection rate

In the pre screening group 69 (1.92%) PJI were identified while in the post screening group it was 131 (1.41%) ($p=0.03$). Table 3 shows the change in infection rate with a significant decrease in the MSSA infection rate ($p<0.0001$), while the non-MSSA infection rate remained the same during the study period. This effect was predominantly in the hip replacement group.

In the pre-screening group of the 69 PJI, 15 (21.7%) cultured multiple organisms (range 2 and 3); while of the 131 PJI in the post-screening group, 30 (22.9%) were multi organism (range 2 and 3).

Table 3
Pre and post screening infections by organism and operation type.

	Prescreening group (2007–2010)			Post screening group (2010–2014)			
	Number	Infection	%	Number	Infection	%	*p* value
Total	**3593**	**69**	**1.92**	**9318**	**131**	**1.41**	**0.03**
MSSA		28	0.75		23	0.25	<0.0001
Non MSSA		**41**	**1.17**		**108**	**1.16**	**0.93**
TKR	1969	21	1.07	5024	67	1.33	0.37
MSSA		**9**	**0.40**		**13**	**0.26**	**0.18**
Non MSSA	12	0.67			54	1.07	0.07
THR	**1624**	**48**	**2.96**	**4293**	**64**	**1.49**	**0.0002**
MSSA		19	1.17		10	0.23	<0.0001
Non MSSA		**29**	**1.79**		**54**	**1.26**	**0.12**

Regression analysis

A multivariate logistic regression model for predictors of MSSA PJI (including deep and superficial infection) was constructed. The significant variables were LOS (coefficient = 0.095, 95%CI 0.060 to 0.131, $p < 0.001$), BMI (coefficient = 0.100, 95%CI 0.044 to 0.156, $p < 0.001$) and MSSA screening programme (odds ratio = 0.407, 95%CI 0.190 to 0.873, $p = 0.02$). The multivariate model for overall infection (deep and superficial infection with any organism) showed that the significant predictors were LOS (coefficient = 0.102, 95%CI 0.078 to 0.126, $p < 0.001$), BMI (coefficient = 0.090, 95%CI 0.062 to 0.118, $p < 0.001$) and hip replacement (odds ratio = 1.66, 95%CI 1.165 to 2.365, $p = 0.005$).

Cost analysis

The average cost of screening is £8 per patient with a total cost of £74,544 (9318 patients). Approximately 20% of these patients would be MSSA positive (20,26), the cost of treating these would be (including postage of Octenisan and Bactroban) £7.73 per patient with a total cost of £14,409 (1864 patients). The total cost implication of the screening programme has therefore been £88,953.

If the MSSA infection rate remained at 0.75% during the post-screening period, the number of possible MSSA infection would be expected to be 70 instead of 23 that was noted in the post surveillance group. Therefore the screening programme prevented a possible 47 patients from having MSSA infection. Thus the average cost of avoiding each infection can be estimated to be £1893 (£88,953/47).

Discussion

In a cohort of 12,911 patients over the study period where data was prospectively collected we have found a significant decrease in the MSSA infection rate after the introduction of the screening program, with an additional decrease in the overall infection rate from 1.9% to 1.4% ($p = 0.03$). This decrease was predominantly in the hip replacement group (3% to 1.5%, $p = 0.002$). We have estimated it to be at a cost saving of £1893 per expected infection.

MRSA screening and decolonising has been universally adopted in England by government mandate and has demonstrated a decrease in MRSA surgical site infection rate.[24] Decolonisation is low cost via nasal mupirocin (Bactroban) ointment and an octenidine (Octenisan) shower on the day of or day before surgery being the recommendation. Despite the focus on MRSA, S. aureus species remain a common cause of prosthetic joint infection, almost always being MSSA. After the introduction of the MSSA decolonisation programme we have noted a three-fold reduction in the MSSA infection rate from 0.75% to 0.25% ($p < 0.0001$). In 2010 Bode et al[20] showed that identification of S. aureus nasal carriers by means of a rtPCR assay, followed by decolonising patients who were carriers of MSSA resulted in reduced rates of surgical site infection. The inclusion criterion for screening was the expectation that a patient would remain hospitalised for at least four days in one of the participating departments (internal medicine, cardiothoracic surgery, vascular surgery, orthopedics, gastrointestinal surgery, or general surgery). Across the whole cohort of patients they reported that the rate of S. aureus infection in carriers was 3.4% (17 of 504) in the decolonised group compared to 7.7% (32 of 413) in the placebo group. This was a significant reduction ($p = 0.008$) with a relative risk of infection, 0.42 (95% confidence interval (CI), 0.23–0.75) in the decolonised group. The study, however, only included 135 orthopaedic patients of whom 95 had hip or knee replacement. We have demonstrated the benefit of this programme in a much larger group of orthopaedic patients (12,911) undergoing primary joint replacement. MSSA screening does remain a contentious issue and the most recent international consensus statement of PJI chose to not recommend universal decolonisation of all patients by a majority of 85%.[24] A review of the literature published in the same year shows Level II–IV evidence for decolonisation from 19 studies[25] along with MRSA screening and decolonisation is now included in WHO guidelines.[26]

The screening programme does add to the overall cost of the preoperative optimization process, but the economic burden of PJI counters this. In the cost benefit analyses that we have performed this has come at a cost of £1893 per S. aureus infection prevented. Financial analyses of revision arthroplasty have revealed the mean cost per septic revision in the UK is £21,937.[9] We have therefore been able to save a substantial amount over the study period with an estimated total cost benefit of £1,031,039 (21,937 × 47) in terms of reduction of costs of managing these infections. Subsequent to the 2010 publication by Bode et al, a subgroup analyses was performed by the authors[22] which showed that the decolonised orthopaedic patients cost €955 less than non-treated patients ($n = 135$, €6097 vs €7052, $p = 0.05$). As is apparent there is potential for large amount of cost saving, if this is accepted through the NHS.

PJI infection is complex and multifactorial. In multivariable logistical regression modelling hospital length of stay, BMI and having a hip operation all emerged as significant independent predictors for all infections. While multivariate analysis showed that MSSA screening programme was a significant factor in preventing MSSA infection, a univariate analysis was shown to significantly reduce overall infection rate ($p = 0.03$). A number of strategies have been implemented at our institution with the aim of reducing length of stay following primary arthroplasty which has fallen significantly in recent years. It is therefore difficult to conclude whether length of stay was a true risk factor for the development of PJI when also modelling for MSSA screening which was is itself defined according to two time periods. We did note that the

knee replacement cohort did not have a proportionate benefit from the screening programme with no change in overall infection rate (1.07% vs 1.33%, $p = 0.37$) or MSSA infection rate (0.40% vs 0.26%; $p = 0.18$). This is difficult to explain, we have not come across anything in the literature to prove why MSSA screening and decolonisation would be more effective in hips than in knees.

Understandably in an age of concern over antibiotic resistance the wide spread use of antibiotics pre operatively must be evidence based. In the population undergoing arthroplasty surgery topical antibiotics are used for short defined lengths and it is unlikely in this setting that a person will be exposed to multiple courses in a short period of time limiting the risk of selecting for resistant organisms. PJI is often treated with prolonged courses of antibiotics and an effective screening programme may be of benefit in preventing antibiotic resistance, but re-colonisation and resistance have proven to be a problem in institutions seeking to eradicate MRSA.[27] The raise is community acquired resistant S. Aureus infections also supports our selective use of decolonization, rather than universal treatment. Our microbiology department routinely monitors MSSA sensitivities and has not reported a significant rise in resistance to mupirocin, since the introduction of this screening and treatment protocol. In our institution the current protocol does not include the routine rescreening of patients on admission for elective joint surgery following decolonisation. This decision was taken as MSSA positive patients would have had 5 days of treatment pre admission and protocolled to continue with nasal treatment for 5 days following surgery therefore repeat screening would have only added costs to the screening program without changing the management of the patient. It has however been shown in previous work that the protocol used in our institution is effective in reducing the carriage rates of MSSA.[28] Whether some of these patients continued to be positive for MSSA despite treatment is unknown and of course whether this contributed to some MSSA infection in the post screening programme cohort is difficult to exclude or confirm.

Demographic data was obtained from our submissions to the National Joint Registry. Between the two groups there was a significant change in compliance with data entry for example BMI entry went from 44.2% in the prescreening group to 83.2% in the post screening group. A key limitation of our study was that the groups were not randomised and improvement in infection rates could have been down to other factors. However, a sufficiently powered randomised control trial to demonstrate a 0.5% difference (as we report) in PJI would require 3000 patients in each arm. The dramatic reduction in MSSA SSI ($p < 0.0001$) compared to the non MSSA SSI ($p = 0.93$) suggests that screening and decolonisation was responsible. Another limitation was that we have not reported on the number of patients who were positive for MSSA carriage during the study period. However, we have clearly noted the benefit of this "intention to treat" screening programme with a significant reduction in MSSA positive infection and the overall infection rate in this group of patients undergoing primary joint replacement. The cost-benefit analyses demonstrates the potential saving that we have made over the study period in economic terms not withstanding the benefits in terms of social, emotional and personal suffering.

In conclusion this study represents the largest case series in the literature so far detailing the effects off MSSA screening and decolonisation. We have shown a significant improvement in both MSSA following the introduction of screening and that significant cost savings have resulted from the programme.

Conflict of Interest

No conflict of interest to declare.

Funding and transparency statement

None of the study authors have received any financial inducement in relation to the preparation of this manuscript. As the corresponding author, I can confirm I have had full access to the data relating to this manuscript and take responsibility for its accuracy and publication

Ethics approval

Local ethics approval received for use and publication of data

Authors contributions

Edward Jeans: Data collection, literature review, data analysis and manuscript preparation

Richard Hollymann: Data analysis and interpretation

David Tait: Data interpretation and microbiology advise

Mike Reed: Study design, literature search and data interpretation

Ajay Malviya: Senior author, study design, manuscript preparation and data interpretation

References

1. Kurtz S, Mowat F, Ong K, Chan N, Lau E, Halpen M. Prevalence of primary and revision total hip and knee arthroplasty in the United States from 1990 through 2002. *J Bone Joint Surg Am* 2005;**87**(7):1487–97.
2. Kurtz S, Mowat F, Ong K, Lau E, Halpen M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am* 2007;**89**(4):780–5.
3. Coello R, Charlett A, Wilson J, Ward V, Pearson A, Borriello P. Adverse impact of surgical site infections in English hospitals. *J Hosp Infect* 2005;**60**(2):93–103.
4. National joint registry England, Wales and Northern Ireland 2015. njrcentra.org.uk.
5. Klouche S., Sariali E., Mamoudy P.. Total hip arthroplasty revision due to infection: a cost analysis approach. *Orthop Traumatol Surg Res* 2010;**96**(2):124–32.
6. Mahomed N.N, Barrett JA, Katz JN, Philips CB, Losina E, Lew RA, Guadagnoli E, Harris WH, Poss R, Baron JA. Rates and Outcomes of Primary and Revision Total Hip Replacement in the United States Medicare Population. *J Bone Joint Surg Am* 2003;**85**(1):27–32.
7. Bozic KJ, Kamath AF, Ong K, Lau E, Kurtz S, Chan V, Vail TP, Rubash H, Berry DJ. Comparative Epidemiology of Revision Arthroplasty: Failed THA Poses Greater Clinical and Economic Burdens Than Failed TKA. *Clin Orthop Relat Res* 2015;**473**(6):2131–8.
8. Peel TN, Cheng AC, Lorenzo YP, Kong DC, Buising KL, Choong PF. Factors influencing the cost of prosthetic joint infection treatment. *J Hosp Infect* 2013;**85**(3) 213-9.
9. Vanhegan IS, Malik AK, Jayakumar P, Ul Islam s, Haddah FS. A financial analysis of revision hip arthroplasty: the economic burden in relation to the national tariff. *J Bone Joint Surg Br* 2012;**94**(5):619–23.
10. Miller KD, Siegel RL, Lin CC, Mariotto AB, Kramer JL, Rowland JH, Stein KD, Alteri R, Jemal A. Cancer treatment and survivorship statistics, 2016. *CA Cancer J Clin* 2016;**66**(4):271–89.
11. Patel H, Khoury H, Girgenti D, Welner S, Yu H. Burden of Surgical Site Infections Associated with Arthroplasty and the Contribution of Staphylococcus aureus. *Surg Infect* 2016;**17**(1):78–88.
12. Hickson CJ, Metcalf D, Elgohari S, Oswald T, Masters JP, Rymaszewska M, Reed MR, Sprowson AP. Prophylactic antibiotics in elective hip and knee arthroplasty: an analysis of organisms reported to cause infections and National survey of clinical practice. *Bone Joint Res* 2015;**4**(11):181–9.
13. Nathwani D, Morgan M, Masterton RG, Dryden M, Cookson BD, French G, Lewis D. British Society for Antimicrobial Chemotherapy Working Party on Community-onset MRSA Infections. Guidelines for UK practice for the diagnosis and management of methicillin-resistant Staphylococcus aureus (MRSA) infections presenting in the community. *J Antimicrob Chemother* 2008;**61**(5):976–94.
14. Johnson R, Jameson SS, Sanders RD, Sargant NJ, Muller SD, Meek RM, Reed MR. Reducing surgical site infection in arthroplasty of the lower limb: A multi-disciplinary approach. *Bone Joint Res* 2013;**2**(3):58–65.
15. Huang S, Platt R. Risk of methicillin-resistant Staphylococcus aureus infection after previous infection or colonization. *Clin Infect Dis* 2003;**36**(3):281–5.
16. Kim D, Spencer M, Davidson SM, Li L, Shaw JD, Guiczynski D, Hunter DJ, Martha JF, Miley GB, Parazin SJ, Dejoie P, Richmond JC. Institutional prescreening for detection and eradication of methicillin-resistant Staphylococcus aureus in patients undergoing elective orthopaedic surgery. *J Bone Joint Surg Am* 2010;**92**(9):1820–6.
17. Stenehjem E, Crispell EK, Rimland D, Farley MM, Satola SW. Longitudinal evaluation of clinical and colonization methicillin-resistant Staphylococcus aureus isolates among veterans. *Infect Control Hosp Epidemiol* 2015;**36**(5):587–9.

18. Sporer SM, Rogers T, Abella L. Methicillin-Resistant and Methicillin-Sensitive Staphylococcus aureus Screening and Decolonization to Reduce Surgical Site Infection in Elective Total Joint Arthroplasty. *J Arthroplasty* 2016;**31**(9 Suppl):144–7.
19. Bode LG, Kluytmans JA, Wertheim HF, Bogaers D, Vandenbroucke-Grauls CM, Roosendaal R, Troelstra A, Box AT, Voss A, van der Tweel I, van Belkum A, Verbrugh HA, Vos MC. Preventing surgical-site infections in nasal carriers of Staphylococcus aureus. *N Engl J Med* 2010;**362**(1):9–17.
20. Moroski NM, Woolwine S, Schwarzkopf R. Is Preoperative Staphylococcal Decolonization Efficient in Total Joint Arthroplasty. *J Arthroplasty* 2015;**30**(3):444–6.
21. van Rijen MM, Bode LG, Baak DA, Kluytmans JA, Vos MC. Reduced costs for Staphylococcus aureus carriers treated prophylactically with mupirocin and chlorhexidine in cardiothoracic and orthopaedic surgery. *PLoS One* 2012;**7**(8).
22. Protocol for the Surveillance of Surgical Site Infection. Version 6, June 2013. Public Health England.
23. Chen AF, Wessel CB, Rao N. Staphylococcus aureus screening and decolonization in orthopaedic surgery and reduction of surgical site infections. *Clin Orthop Relat Res* 2013;**471**(7):2383–99.
24. Parvizi J, Gehrke T, Chen AF. Proceedings of the International Consensus on Periprosthetic Joint Infection. *Bone Joint J* 2017;**95B**(11):1450.
25. Leaper DJ, Edmiston CE. World Health Organization: Global guidelines for the prevention of surgical site infection. *J Hosp Infect* 2017;**96**(1):20–1.
26. Kauffman CA, Terpenning MS, He X, Zarins LT, Ramsey MA, Jorgensen KA, Sottile WS, Bradley SF. Attempts to eradicate methicillin-resistant Staphylococcus aureus from a long-term-care facility with the use of mupirocin ointment. *Am J Med* 1993;**94**(4):371–8.
27. Zetola N, Francis JS, Nuermberger EL, Bishai WR. Community-acquired methicillin-resistant Staphylococcus aureus: an emerging threat. *Lan Infect Diseases* 2005;**5**(5):275–86.
28. Chen AF, Heyl AE, Xu PZ, Rao N, Klatt BA. Preoperative Decolonization Effective at Reducing Staphylococcal Colonization in Total Joint Arthroplasty Patients. *J Arthroplasty* 2013;**28**(8):18–20 Suppl.

EXHIBIT DX11

TO DECLARATION OF BENJAMIN W. HULSE IN SUPPORT OF DEFENDANTS' MOTION FOR RECONSIDERATION OF THE COURT'S DECEMBER 13, 2017 ORDER ON GENERAL CAUSATION

Report of Jonathan Borak, MD, DABT

Re: Nancy J. Axline

September 4, 2018

I. Introduction

1. This report addresses issues of specific causation as they relate to the prosthetic joint infection (PJI) suffered by Ms. Nancy J. Axline following left hip arthroplasty in April 2009. I have previously provided two expert reports (the first dealing with general causation and the second with specific causation for a different plaintiff), several supplemental reports, and testimony in two depositions and a trial, all responsive to related matters. Those earlier reports and testimony, including exhibits and citations, are hereby incorporated into my current report.

2. I am Clinical Professor of Medicine at Yale University, a faculty member of the Yale Occupational and Environmental Medicine Program, and Adjunct Associate Professor of Medicine at The Johns Hopkins University. I am also President of Jonathan Borak & Company, a consulting firm in New Haven, Connecticut. I am or have been a member of numerous national advisory panels, an officer or director of numerous medical and scientific organizations, an editorial board member or peer reviewer of numerous medical and scientific journals, and the author of numerous books, book chapters and peer reviewed publications. My current CV is attached as an appendix.

II. Materials Reviewed

3. In the present matter, I was asked by Mr. Corey Gordon of Blackwell Burke to review the following medical records, expert reports, and depositions:

Ms. Axline's medical records (listed alphabetically)

Harding Memorial Healthcare
Joint Implant Surgeons, Inc.
Marion Area Health Center
Marion General Hospital
Marion Orthopedic, Inc.
Mount Carmel Hospital
Meijer Pharmacy
Walgreen Pharmacy

Deposition transcripts (listed alphabetically)

Ms. Nancy J. Axline (07/10/2018)
Mr. Ronald Axline (07/10/2018)

Dr. Adolph V. Lombardi (08/01/2018)
Dr. Nestor M. Narcelles (07/23/2018)
Dr. James H. Smith, (06/28/18)

Expert Reports

William R. Jarvis, MD (08/13/2018)

4. I also reviewed a large number of scientific reports related to surgical warming devices, operating room procedures, risk factors for surgical complications and infections, and other related medical and scientific issues. Specific publications are cited in this report and in my earlier reports and deposition. I have also attached a cumulative reference list of the medical and scientific literature that I have reviewed in the context of this and related matters.

5. I understand that there may be additional depositions and further discovery in this matter, and I reserve the right to amend or supplement my report in light of any additional records or evidence that become available. Likewise, the medical literature is dynamic and changing and therefore I reserve the right to amend or supplement my report in light of any additional medical or scientific evidence of which I become aware.

III. Background

6. Ms. Axline (DOB: 12/28/56) underwent left total hip arthroplasty (THA) on 04/21/09 for treatment of degenerative joint disease. She had undergone right hip arthroplasty in 2008. The 4/21/09 anesthesia record [AXLINEN-32-MCEH-00458] documents that: she was obese (Ht: 5'5"; BW: 199.6 lbs, BMI: 33.3); her American Society of Anesthesiologists (ASA) score was 3; and she received 2 grams of Cefazolin (Ancef) IV as pre-operative prophylaxis. Her core temperature was stable throughout the surgery (temp 35.7-35.8C); she did not experience a significant temperature decline and recovery as has been associated with anesthesia without active warming. She was discharged from hospital on 04/24/09.

7. Post-operatively, Ms. Axline was "doing well" for several weeks but then developed a rash on her left leg and "severe pain" in the left groin and knee [AXLINEN-18JIS-00019]. She was seen again on 06/12/09 with a complaint of more severe pain of left hip and thigh and limited ability to ambulate [AXLINEN-18JIS-00016]. She was again seen on 07/02/09 with continued pain [AXLINEN-18JIS-00013]. Evaluation for possible PJI indicated an elevated ESR (55; normal <30) and CRP (55; normal <9) [AXLINEN-10PPR-00075]. She was next examined on 07/31/09 at which time it was proposed that she undergo surgery for revision of the hip prosthesis; her ESR was then 69, her CRP was 73.7, and aspiration of her hip on 8/04/09 documented the presence of coagulase positive Staph aureus sensitive to methicillin [AXLINEN-10PPR-00076]. Accordingly, she was diagnosed as having a left hip PJI and she underwent treatment with intensive antibiotics, surgical removal of the prosthesis on 08/21/09, and a two-stage revision and reimplantation.

8. In addition to osteoarthritis and a history of prior surgery, Ms. Axline's medical history prior to 04/21/09 was remarkable for obesity, anemia, hypothyroidism, substance abuse (opioids and alcohol), hypertension, dyslipidemia, and depression.

8a) Ms. Axline had longstanding obesity. The following table indicates her body weight and body mass index (BMI) as documented in her medical records prior to her left THA.

Table 1: Ms. Axline's weight and BMI

Date	Weight (lb)	BMI*	Source
04/21/94	201	33.4	20HMH-00140
07/11/97	218.6	36.4	20HMH-00138
06/09/01	207	34.4	20HMH-00133
08/25/03	206	34.3	20HMH-00129
05/04/07	219	36.4	20HMH-00101
02/07/08	215	35.8	33MCEH-00628
04/21/09	199.6	33.2	32MCEH-00458

(*calculations assume height of 65") [1]

In addition, she testified that her primary care physician, Dr. Husain, repeatedly described her as obese:

> **Q.** … your weight's 170 something now, what was it at its highest?
> **A.** Probably 200, a little over 200. I can't remember.
> **Q.** Did anybody ever diagnose you with … obesity?
> **A.** Dr. Husain used to do that, even when I would be like 180, he would say that was technically obese.[2] [Depo p.194]

8b) Ms. Axline had hypochromic, microcytic anemia that was apparently first documented in 02/08, at the time of her initial THA. The earliest complete blood count (CBC) from that hospitalization (02/08/08) indicated low levels of hemoglobin (HgB = 10.5), hematocrit (Hct = 31.5), mean corpuscular volume (MCV = 79), and mean corpuscular hemoglobin (MCH = 26.5) [33MCEH-00648]; those values are consistent with iron deficiency anemia. I found no indication that the anemia was evaluated or treated at that time.

In late 2008, Ms. Axline underwent medical assessment for her second THA scheduled for January 2009. Testing on 12/23/08 documented "Significant Anemia" and severe iron deficiency [20HMH-00066;-00067] (see table below). She was found to have gastritis and colonic diverticula, but no source of blood

[1] BMI is calculated in the metric system as [kg/m^2], with body weight in "kg" units and height in "m" units. Calculation in the English system is less intuitive. It is calculated as weight in "lbs" units divided by height squared in "inch" units, all multiplied by 703. Thus in the English system, BMI = [(lbs/in^2) x 703] (1).

[2] For women 5'5" tall, a body weight of 180 lbs. is equivalent to a BMI of 30, the definition of "obesity".

loss was identified. Her surgery was delayed and she was treated with iron supplements. Serial CBCs indicated response to treatment, but abnormalities persisted up to and after the April 2009 surgery (see table below). On 08/21/09 she underwent surgical removal of the prosthesis; she had significant hypochromic, microcytic anemia and she was transfused with one unit of packed red blood cells [32MCEH-00284, -00404]. I found no indication that her anemia was further evaluated or treated. Prosthesis reimplantation was performed on 10/05/09, when she was again noted to have significant anemia [18JIS-00049]. Moreover, as noted in the table below, significant iron deficiency and anemia have persisted at least through early 2018 [20MCEH-000348; -00036; 00035; 00031; 00026].

Table 2: Ms. Axline's hematological test results [3]

Date	HgB	HCT	MCV	MCH	RDW	Serum Fe	TIBC	Fe Saturation
02/08/08	10.5	31.5	79	26.5	14.2			
12/23/08	9.9	30.4	71	23.1	17.7	5	320	`5%
01/23/09	12.3	37.3	76.4	25.3	24.5			
02/12/09	13.7	41.2	79.8	26.6	25			
04/21/09	13.7							
04/22/09	11.5	34.3	88	29.5	13			
04/24/09	10.1	30.1	89	29.8	12.9			
08/21/09	9.3							
08/22/09	8.3	25.2	77	25.5	15.3			
10/05/09	7.6	24						
06/06/12	13.7	40	89	30.4	12.3			
10/12/14	7.5	25.5	60	17.8	18.3			
06/22-23/16	8.3	27.6	65	19.7	30.2	11	473	2%
04/24/17						38	369	10%

In summary, Ms. Axline's laboratory results indicate that she had significant iron deficiency and anemia that was persistent and unexplained. At the time of her THA on 4/21/09, her hemoglobin level was normal, presumably because she had taken iron supplements for several weeks in early 2009. However, her blood testing indicated anemia the following day and she remained anemic until June 2012. The cause of her iron deficiency was neither explained nor corrected. She testified that she also took iron supplements for about two weeks at an unspecified later time [Depo p.108-113], which I presume was in 2012, when her HgB briefly returned to the normal range. With those two exceptions, her iron levels and her CBC showed persistent deficiencies from at least 2008 through 2017.

[3] Following are the normal ranges for these tests as reported by Medical Carmel East Hospital and/or Harding Memorial Healthcare: HgB: 11.5- 17 g/dL; HCT: 34-50%; MCV: 80-98 fL; MCH: 27-34 pg; RDW: 11.7-15%; Serum Fe: 45-160 µg/dL; TIBC (Total Iron Binding Capacity) 250-450 µg/dL; Fe Saturation: 11-50%.

She denied symptoms or knowledge about her persistent iron deficiency and on-going anemia, although her primary care provider (S. Wynn, PA-C) repeatedly noted the presence of iron deficiency and anemia in her medical records.

8c) Ms. Axline was diagnosed as hypothyroid in 1996 [33MCEH-00612; -00443]. I found no description of the underlying cause of her thyroid dysfunction or the results of her original thyroid evaluation. She was treated with thyroid hormone replacement (levothyroxine, Synthroid) with doses that varied between 50 and 175 µg/day. During those years, her thyroid function was sometimes apparently well treated, but at other times she seemingly received too much or too little Synthroid.[4] I found no evidence that her thyroid function was evaluated during the 4-plus months prior to her 4/21/09 THA.

Table 3: Ms. Axline's TSH levels

Date	TSH level	Source
09/14/00	10.85	20HMH-00080
07/23/07	3.1	20HMH-00071
12/10/08	0.58	20HMH-00069
11/24/09	0.22	20HMH-00058
09/17/12	3.64	20HMH-00055
06/18/14	20.44	20HMH-00051
10/15/14	17.36	20HMH-00050
11/12/14	1.2	20HMH-00044
01/10/18	0.43	20HMH-00030

8d) Ms. Axline had been diagnosed with alcohol and drug abuse [29MGH-00022], although I found no evidence that she had been addicted. Her personal record contains multiple episodes of public intoxication and multiple convictions for DUI. She was first convicted in 1988 [Ohio Case 88TRC05503]. Her second conviction was in 2004, her license was suspended and she was sentenced to jail [29MGH-00028; TRC0408804A]. In 2011, she was again convicted, her license was again suspended and she was sentenced to six months in jail [TRC1100438A]. In 2017, she was convicted twice for alcohol-related offenses. First, she pleaded guilty in January to disorderly conduct while intoxicated [CRB1700208]. Then, in December, she was convicted of physical control of a vehicle while intoxicated and was again sentenced to jail time [TRC1708670A]. In addition, on 8/25/07 she was treated at Marion General Hospital for Cymbalta overdose and acute ethanol intoxication. At that time, testing was also positive for marijuana and a history of alcohol abuse was noted [29MGH-00007, -00014; -00022; -00024; -00028]. In summary, Ms. Axline

[4] The adequacy of thyroid replacement is generally monitored by consideration of serum Thyroid Stimulating Hormone (TSH), which varies inversely with the serum thyroid hormone levels (2). The normal range, as reflected in the Harding Memorial Healthcare records, is about 0.35-5.0 mU/L: levels >5.0 mU/L suggest under-treatment and levels <0.35 mU/L suggest overtreatment. However, a just-published meta-analysis of 99 studies indicates that markers of hypothyroid-associated metabolic abnormalities "remain different despite normalization of serum TSH on LT4 [levothyroxine] monotherapy" (3). Thus normalization of TSH does not necessarily indicate normalization of thyroid function.

has a history of chronic alcohol abuse with numerous convictions related to public intoxication despite repeated suspensions of her driving license, repeated sentences for jail time, and repeated monetary fines.

It is also notable that Ms. Axline took opioids (oxycodone and tramadol) during the three months prior to her 4/21/09 surgery. At that time, she also manifested drug seeking behavior, i.e., seeking opioid prescriptions from multiple physicians. Her Meijer Pharmacy records indicate that between 12/30/08 and 4/21/09 she filled prescriptions for 90 tabs of codeine, 240 tabs of oxycodone, and 50 tabs of tramadol [37MEP-00002]. The codeine and oxycodone had been prescribed by Dr. Husain, her primary care physician, and the tramadol by Dr. Lombardi, her orthopedic surgeon. Dr. Lombardi testified that he had no record that she was also receiving opioids from Dr. Husain and that he would not have prescribed opioids for her if he had known because "opioid-dependent patients can be an extreme challenge" [Depo p.26-9]. In the addiction field, seeking opioids from multiple prescribers is sometimes referred to as a "red flag".[5]

8e) Ms. Axline had hypertension that was first diagnosed in 2001 and for which was being treated with selective beta blockers such as metoprolol.

8f) Ms. Axline had hyperlipidemia (elevated cholesterol and triglycerides), for which she was treated with statin medications.

8g) Ms. Axline had been diagnosed as suffering depression, for which she was treated with various selective serotonin reuptake inhibitor (SSRIs) including Lexapro, Cymbalta and Paroxetine.

III. Discussion

A. Obesity and Prosthetic Joint Infections

9. Obesity is a well-established risk factor for PJI, an association that has been repeatedly documented. Numerous published studies have considered that association, but most have been relatively small and underpowered. Accordingly, my earlier reports focused on the results of four recent meta-analyses that aggregated the findings of those smaller studies, thus addressing concerns about limited statistical power (4-7). Those meta-analyses, conducted using appropriate and documented methods, indicated that obesity is a significant, independent risk factor for PJI and that risks increase as BMI increases over 30. The meta-relative risks were generally >2, ranging up to 5.06. Stronger associations were found in the studies of higher methodological quality and those that focused on total knee and hip replacements.

10. Recent reports continue to document that pre-surgical obesity is a significant risk for PJI. Following are five examples:

[5] For example, see: *Interagency Guideline on Prescribing Opioids for Pain* at: http://www.agencymeddirectors.wa.gov/files/2015amdgopioidguideline.pdf.

10a) Tan et al 2016 (8) and Tan et al 2018 (9) reported the results of a retrospective analysis of 43,253 TJAs performed in 27,717 patients treated between 2000 and 2014 at a single university hospital. Data were obtained from an institutional database which included the patients' preexisting comorbidities. Cases included both primary and revision TJAs. All records were searched electronically and then manually. Results included unilateral risk estimates for each of 17 risk factors that were significantly associated with PJI and the weighted rankings of individual risk factors based on multivariate risk calculation, with results subjected to external validation. There were 1035 cases of confirmed PJI.

Obesity (defined as BMI > 30) was significantly associated with PJI in univariate analyses (OR: 1.49; 95% CI: 1.24-1.79). In multivariate analyses, its association with PJI was highly significant ($p < 0.001$): "It is important to note that the risk of PJI increased as the BMI either increased or decreased from a nadir at 29.3 kg/m^3".

10b) Bozic 2012 (10) analyzed a 5% national sample of the Medicare database, considering relative risk of PJI after 30 days post-operative in 40,919 patients who underwent primary THA between 1998 and 2007. PJI was identified as "ICD-9-CM diagnosis code 996.66 (infection resulting from an internal joint prosthesis)". Obesity and other pre-operative comorbid conditions were compiled from diagnoses (based on ICD9 codes) included in either Part A (inpatient) or Part B (outpatient) claims submitted during the twelve-month period prior to the THA. Analyses were adjusted for multiple comparisons.

Multivariate analyses were performed that included 29 comorbid conditions as well as age, sex and race. For obesity, the unadjusted relative risk was 1.97 (95% CI: 1.57-2.48) and the adjusted risk was 1.73 (95% CI: 1.35- 2.22). These results were highly significant (adjusted $p = 0.0014$).

10c) Bozic et al. 2012 (11) performed a similar analysis that focused on 83,011 patients who underwent primary TKA. Obesity and other pre-operative comorbid conditions were compiled from diagnoses (based on ICD9 codes) included in either Part A (inpatient) or Part B (outpatient) claims submitted during the twelve-month period prior to the TKA. Analyses were adjusted for multiple comparisons.

Obesity was a significant independent risk factor for PJI. The unadjusted relative risk was 1.38 (95% CI: 1.19-1.59) and the adjusted risk was 1.22 (95% CI: 1.03-1.44). These results were statistically significant (adjusted $p = 0.0219$).

10d) Lenguerrand et al (12) analyzed the National Joint Registry for England and Wales, Northern Ireland and the Isle of Man between 04/01/03 and 12/31/13. They focused on the risks of revision for PJI after THA. There were a total 623,253 THA patients followed-up for at least one year. Surgical revision for PJI was performed in 2,705 patients. Comorbid conditions and other risk factors were obtained from linked national medical and hospital databases.

Univariate and multivariate analyses were performed including age, sex, ethnicity, and more than 20 comorbid factors. Compared to those with BMI <25, risk of PJI in patients with BMI ≥ 30 was significantly increased ($p < 0.05$) with a two-fold increase in the incidence rate per thousand person-years (1.82 vs. 0.91; $p < 0.05$).

10e) Bell 2018 (13) analyzed the risks of PJI in 23,754 patients who underwent TJA between 1/1/05 and 1/31/17 at the same university hospital studied by Tan et al (9). The overall PJI rate was 0.98%. Univariate and multivariate analyses were performed that included age, sex, race and a large number of comorbid conditions. Obesity was defined as BMI >30 and PJI was defined by the "Musculoskeletal Infection Society criteria for PJI". The association between obesity and PJI was highly significant (adjusted OR: 1.58; 95% CI: 1.19-2.08; p <0.001).

11. As discussed in my earlier reports and depositions, obesity has also been shown to be a significant risk factor for post-operative surgical infections across a variety of surgical procedures not necessarily involving the implantation of orthopedic appliances.

B. Anemia and Prosthetic Joint Infections

12. Pre- and post-operative anemia are recognized as independent risk factors for complications, mortality and quality of life following orthopedic and other surgical procedures (14-16). The presence of pre-operative anemia has been specifically associated with significantly increased risk of PJI in TJA patients.

12a) Greenky et al. 2012 (17) evaluated the records of 15,222 patients who underwent TJA between 1/00 and 6/07 treated at a single university hospital. Those with acute trauma or known PJI were excluded. Patients were followed for at least 3 years post-operatively. Anemia was diagnosed by CBC testing 3-6 weeks pre-operatively; anemia was defined as Hgb <12 g/dL in women and Hgb <13 g/dL in men. There were 2,991 with anemia and 12,231 without.

Risk of PJI was significantly greater in anemic patients (4.3% vs. 2%; p<0.01). In multivariate analyses, risk of PJI was significantly greater in those with anemia (OR, 1.88; 95% CI, 1.38–2.56; $p < 0.001$). Fully-adjusted multivariate analysis found even greater risk in anemic patients (OR, 1.95; 95% CI, 1.41–2.69; p <0.001).

12b) Tan et al 2016 (8) and Tan et al 2018 (9) reported the results of a retrospective analysis of 43,253 TJAs performed in 27,717 patients treated between 2000 and 2014 at the same hospital where the Greenky study was undertaken. Data were obtained from an institutional database which included the patients' preexisting comorbidities. Cases included both primary and revision TJAs. All records were searched electronically and then manually. Results included unilateral risk estimates for each of 17 risk factors that were significantly associated with PJI and also the weighted ranking of individual risk factors based on a multivariate risk

calculation, with results subjected to external validation. There were 1035 cases of confirmed PJI.

Iron deficiency anemia was significantly associated with PJI in univariate analyses (OR: 1.74; 95% CI: 1.48-2.05). In the multivariate analysis, its association with PJI was highly significant ($p < 0.0001$).

12c) Bozic et al. 2012 (10) analyzed a 5% national sample of the Medicare database, considering relative risk of PJI after 30 days post-operative in 40,919 patients who underwent primary THA between 1998 and 2007. PJI was identified as "ICD-9-CM diagnosis code 996.66 (infection resulting from an internal joint prosthesis)". Pre-operative anemia and other comorbid conditions were compiled from diagnoses (based on ICD9 codes) included in either Part A (inpatient) or Part B (outpatient) claims submitted during the twelve-month period prior to the THA. Analyses were adjusted for multiple comparisons.

Multivariate analyses were performed that included 29 comorbid conditions as well as age, sex and race. For anemia, the unadjusted relative risk was 1.61 (95% CI: 1.37-1.90) and the adjusted risk was 1.36 (95% CI: 1.15- 1.62). These results were statistically significant (adjusted $p = 0.0347$).

12d) Bozic et al. 2012 (11) performed a similar analysis that focused on 83,011 patients who underwent primary TKA. Anemia, diagnosed within 30 days of surgery, identified in diagnoses (based on ICD9 codes) included in either Part A (inpatient) or Part B (outpatient) claims submitted during the twelve-month period prior to the TKA. Analyses were adjusted for multiple comparisons.

Anemia was a significant independent risk factor for PJI. The unadjusted relative risk was 1.39 (95% CI: 1.23-1.58) and the adjusted risk was 1.26 (95% CI: 1.09-1.45). These results were statistically significant (adjusted $p = 0.0013$).

I am not aware of any evidence that short-term correction of anemia (e.g., short-term administration of iron or red blood cell transfusion to optimize blood count) normalizes the anemia-associated risks of post-operative infection.

C. Hypothyroidism and Prosthetic Joint Infections

13. Thyroid hormones have been shown to modulate immune function and hypothyroidism has been associated with decreased suppression of cell-mediated immunity and impaired would healing (18-21). Accordingly, the contribution of hypothyroidism to PJI following TJA has been recently evaluated and demonstrated.

13a) Tan et al. 2016 (22) performed a retrospective analysis of 32,289 TJAs identified in 26,427 patients treated at a single university hospital between 01/00 and 01/13. Data were obtained from an institutional database which included the patients' preexisting comorbidities, including hypothyroidism. Among the 32,289

TJA patients, 4008 had a history of hypothyroidism and 28,281 had no such history. In patients with hypothyroidism, TSH levels within 1 month before the index TJA were recorded, but TSH and free thyroxine levels were not routinely obtained prior to surgery.

Of the 4008 TJAs performed in patients with a hypothyroid history, 135 (3.4%) developed PJI, compared to 384 (1.4%) in patients without such a history (unadjusted OR: 2.53). When controlling for potential confounders, the adjusted OR was very significantly increased (adjusted OR: 2.46; 95% CI: 1.99-3.05; p <.0001).

TSH levels were available for 1872 TJA patients, including 894 (22.2%) of those with a history of hypothyroidism. Among patients with an elevated TSH level (>5 mU/L), the PJI rate was 6.1% compared with 3.6% in patients with a normal TSH (OR: 1.76, p = .07).

13b) Buller et al. 2018 (23) performed a retrospective, case-control study using the PearlDiver medical records database of "100% Medicare Standard Analytical Files" from 2005 to 2014. This database included 2,369,594 TKAs and 1,277,014 patients with a diagnosis of hypothyroidism. After matching by age and gender and also randomization, each cohort comprised 98,555 patients. Ninety-day complication rates were tracked using ICD9 coding; PJI and other surgical infections were tabulated separately.

Patients with a diagnosis of hypothyroidism experienced a significantly higher rate of PJI than those without a history of hypothyroidism (OR: 1.502; 95% CI: 1.271-1.775; p <.001).

13c) Althoff et al. 2018 (24) performed a retrospective, case-control study using the PearlDiver medical records database of "100% Medicare Standard Analytical Files" from 2005 to 2013. This database included 6977 patients who underwent Total Ankle Arthroplasty (TAA). There was a history of hypothyroidism in 2010 (28.8%) of the TAA patients. PJI was defined as the "diagnosis of periprosthetic infection or septic ankle and/or a procedure for postoperative infection or septic ankle arthritis" within 6 months of surgery.

There were 294 TAA patients who developed PJI. The risk of PJI was significantly increased in hypothyroid patients after 3 months (OR: 1.27; 95% CI: 1.02-1.58; p = 0.018) and after 6 months (OR: 1.32; 95% CI: 1.03-1.69; p = 0,028).

D. Substance Abuse and Prosthetic Joint Infections

14. Along with their recognized analgesic effects, opioids can interfere with several aspects of normal immune system function (25-27); the mechanisms underlying these effects are not well understood. In animal studies, pretreatment with opioids predisposes to surgical infections, sepsis and mortality. Although less well researched, there are concerns that similar effects could be seen in humans.

Because of such concerns, the risks of PJI associated with preoperative use of opioids have been recently studied by analysis of hospital and health system databases. To understand these studies, it is necessary to appreciate that a diagnosis of "opioid abuse" does not necessarily imply either dependency or addiction. Likewise, that diagnosis does not imply parenteral (e.g., intravenous or IV) use of prescription or illicit drugs. There are separate ICD9 codes for "opiate dependency" and "nondependent opioid abuse", but the distinction is often difficult and the two are sometimes combined for research purposes:

> "… as it often is difficult to distinguish between opioid abuse and dependence in the hospital setting, we decided to combine the two entities for the primary analysis—an approach that is consistent with the definition of "opioid use disorder" in the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5)" (28).

15. Following are summaries of recent studies that demonstrate a significant association between opioid use and PJI.

15a) Memendez et al 2015 (28) performed a retrospective analysis of the Nationwide Inpatient Sample from 2002-2011, a dataset that is maintained by the US Agency for Health Care Research and Quality. The dataset, a 20% stratified sample of discharges from 1000 hospitals, included 9,307,348 hospitalizations for "major elective orthopedic surgery". Among those patients 15,901 (0.2%) were diagnosed as opioid abuse or opioid dependence.

Surgical site infections, including PJI, were very significantly associated with opioid abuse: unadjusted OR: 3.4 (95% CI: 2.8-4.1; p <0.001); fully-adjusted OR 3.2 (95% CI: 2.6-3.9; p <0.001).

15b) Cozowicz et al 2017 (29) analyzed the Premier Perspective database which contains data from ≈ 25% of US hospital discharges 2006-2013, including 1,035,578 elective THAs and TKAs. The primary effect variable was "opioid utilization, defined as perioperative in-hospital opioid prescription" on the day of surgery or the following day. Patients were categorized in quartiles according to their calculated morphine equivalent opioid doses.

Compared to patients in the lowest three quartile categories, those in the highest opioid category had significantly increased risk of postoperative surgical infection (OR: 1.485; 95% CI: 1.236-1.784; p < 0.001).

15c) Bell 2018 (13) analyzed the risks of PJI in 23,754 patients who underwent TJA between 1/1/05 and 1/31/17 at a single university hospital. The overall PJI rate was 0.98%. Univariate and multivariate analyses were performed that included age, sex, race and a large number of comorbid conditions. Opioid users were identified as "those who were currently taking opioids at the last outpatient visit before surgery or

during preadmission testing, as noted in the records." There were 5051 patients who were opioid users and 18703 who were opioid naïve.

The rate of PJI was significantly increased in the opioid users (1.4%; 71/5051) compared to the opioid naïve patients (0.86%; 162/18,703). When adjusted for potential confounders using multivariate analysis, opioid usage remained a significantly increased independent risk factor for development of PJI within 2 years post-operatively (adjusted OR, 1.53; 95% CI, 1.14-2.05; $p = 0.005$).

15d) Cancienne et al. 2018 (30) performed a retrospective analysis of the PearlDiver medical records database from 1/1/07 to 4/1/16. This database, which combines data from Humana and Medicare using ICD9 diagnostic codes and CPT procedural codes, contains about 20 million patients with orthopedic diagnoses. There were 113,337 primary TKA patients with at least 6 months of post-operative follow-up. Preoperative opioid users were defined as "those filling at least one narcotic prescription between 4 months and 1 month prior to the date of TKA". The number of filled narcotic prescriptions during this time was "obtained and divided into 1, 2, 3, or ≥4 preoperative filled prescriptions in the 3-month preoperative time window".

The risk of PJI during the first post-operative year increased with increasing number of narcotic prescriptions. Overall, preoperative narcotic use was very significantly associated with increased risk of PJI within 1 year (OR 1.16; 95% CI: 1.11-1.22; $p <$ .0001).

15e) Tan et al 2016 (8) and Tan et al 2018 (9) reported the results of a retrospective analysis of 43,253 TJAs performed in 27,717 patients treated at a single university hospital between 2000 and 2014. Data were obtained from an institutional database which included the patients' preexisting comorbidities. "Drug abuse" was defined as "any patient with a history or current use, with recent or current use considered an absolute contraindication to elective surgery". All records were searched electronically and then manually. Results included unilateral risk estimates for each of 17 risk factors that were significantly associated with PJI and also the weighted ranking of individual risk factors based on a multivariate risk calculation, with results subjected to external validation. There were 1035 cases of confirmed PJI.

Drug abuse was the most significant individual comorbid risk factor (OR: 6.53; 95% CI: 2.76-13.86). In the multivariate analysis, its association with PJI was highly significant ($p = 0.0003$).

15f) In his testimony, Dr. Lombardi, Ms. Axline's orthopedic surgeon, agreed that use of opioids including oxycodone, one of the medications that Ms. Axline was using, can increase risk of surgical infections:

> Q. ... Was one of the reasons that you preferred not to prescribe preoperatively stronger opioid pain medication like oxycodone the possibility that that would increase a patient's risk of developing a prosthetic joint infection?
> A. There are -- as you are aware, there's multiple reasons why a patient develops infection. There's not one specific reason. There are many reasons why you wouldn't prescribe an oxycodone preoperatively, one of which may be infection ... [Lombardi depo 27-28]

16. There is also substantial evidence that alcohol affects the human immune system: "even moderate amounts of alcohol and binge drinking modulate host immune responses" (31). The mechanisms of many such adverse effects have been demonstrated in experimental studies, but there remain areas of uncertainty regarding their specific dose-relatedness and reversibility:

> "...many aspects of alcohol consumption and its effects on immunity and host defense have not yet been fully elucidated. For example, the pattern of alcohol consumption (e.g., occasional binge drinking versus chronic heavy drinking) may affect the immune system in different ways that are yet to be explored." (31)

> "alcohol consumption alters both innate and adaptive immunity in both humans as well as animal models, however these effects have not been systematically assessed on the basis of the amount of alcohol consumed and duration." (32)

Despite such uncertainties, there is general consensus that alcohol consumption disturbs the immune system, that alcohol abuse leads to immune system dysfunction, and that such disturbance and dysfunction predisposes alcohol consumers to increased risks of infections (31-34).

17. Following are summaries of recent studies that demonstrate a significant association between alcohol use and PJI.

17a) Tan et al. 2016 (22) performed a retrospective analysis of 32,289 TJAs identified in 26,427 patients treated at a single university hospital between 01/00 and 01/13. Data were obtained from an institutional database using ICD9 codes to identify outcomes and risk factors followed by hand searches of medical records. Using multivariate analyses, alcohol abuse was significantly associated with PJI (OR: 1.49; 95% CI: 1.01-2.21; $p = 0.0447$)

17b) Best et al (35) performed a retrospective analysis of the National Discharge Survey, a database of in-patient discharges from non-federal, short stay hospitals maintained by the CDC. The study included 8,372,232 patients without cirrhosis[6] who underwent primary THA or TKA between 1990 and 2007. Alcohol misuse (including both alcohol abuse and alcohol dependence) was identified by ICD9 codes. According to criteria of the American Psychiatric Association criteria), alcohol

[6] Patients with cirrhosis were excluded because it is often associated with alcohol abuse and is itself associated with increased risk of infections.

abuse was defined as including recurrent use of alcohol in situations where it is physically hazardous (e.g., driving an automobile) and recurrent alcohol-related legal problems (e.g., arrests for alcohol-related disorderly conduct).

Of the 8,372,232 patients, 50,861 had a diagnosis of alcohol misuse. In bivariate analyses, alcohol misuse was significantly associated with acute postoperative infection (OR: 15.314; 95% CI: 14.662-15.966; p <0.001) and complications of internal joint prosthesis (OR: 1.545; 95% CI: 1.319-1.810; p <0.001).

17c) Kong et al (36) performed a meta-analysis of 16 cohort or case-control studies that reported the incidence of PJI after THA or TKA. Three of the studies included alcohol abuse among comorbid risk factors. The meta-risk of PJI was significantly increased in alcohol abuse (OR: 1.88; 95%CI: 1.32-2.68; p <0.01).

E. Cumulative Risk Factors and Prosthetic Joint Infections

18. The above sections of this report considered the evidence linking several individual comorbid conditions with an increased risk of PJI. That approach assumes that it is possible to isolate the responsibilities of individual risk factors. However, it seems more probable that each infection results from multiple factors. This is reflected in statements from two expert orthopedic surgeons, Dr. Adolph Lombardi and Dr. Mike Reed.

18a) As quoted above, Dr. Lombardi testified that there are "multiple reasons why a patient develops infection. There's not one specific reason" [Lombardi depo 28].

18b) Dr. Reed, senior author of the McGovern study on which Dr. Jarvis relied, has written that almost all surgical wounds are contaminated at the time of surgery: "It is likely that almost all surgical wounds are contaminated ..." (37).[7] Because PJIs are generally reported in fewer than 2% of patients, it follows that whether a given surgical wound develops infection will depend on a variety of factors (i.e., "multiple reasons"), not simply the possibility of wound contamination.

Accordingly, surgical researchers have considered ways to evaluate and quantify such multiple risks. For example, consider the following:

> "... considerable effort has been made in the past decade to identify risk factors for PJI. Although both modifiable and non-modifiable risk factors have been identified, few studies have effectively reconciled the relative influences of such factors. An effective, validated preoperative tool to quantify the risk of PJI could potentially allow surgeons to intervene before, or even to avoid, operating on

[7] The almost universal prevalence of surgical wound contamination has been observed more generally. For example: "In clean surgery, the wound is often contaminated at closure. The proportion of contaminated wounds in cardiac surgery can be as high as 89%, depending on the type of surgery and the microorganism" (38).

individuals for whom the risk of PJI may outweigh the potential benefits of TJA". (9)

"Multiple clinical risk-stratification classification systems ... have been shown to correlate with the risk of morbidity and mortality in surgical patients... Our study builds on the findings of previous investigators by identifying the specific comorbidities associated with periprosthetic joint infection and with postoperative mortality, thus providing a more clinically meaningful basis for communication between surgeons and patients and for clinical decision-making." (10)

19. To illustrate the use of such a risk calculator for PJI, I accessed the Total Joint Replacement Risk Calculator (TJRRC) available from the American Joint Replacement Registry, a part of the American Academy of Orthopedic Surgeons Registry Program.[8] The TJRCC was developed using Medicare data. Because Ms. Axline was too young to be part of the Medicare cohort, the calculator cannot quantify her actual risk for PJI, but it provides quantitative perspective on the cumulative nature of her various comorbid conditions and their impact on her relative risk of PJI.

Using TJRRC, I calculated the risks of PJI following TJA in a White woman age 65-69 years and 5'5" in height, according to various combinations of Ms. Axline's comorbid risk factors.[9] In the first calculation I assumed that she was not obese (BMI < 30). In the second calculation I assumed that she was obese (200 lbs; BMI 33.3), but had no other comorbid risk factors. In subsequent calculations, I included her other comorbidities.

	Comorbid Conditions	Average Risk of PJI
1)	Body weight = 175, BMI = 29.1; No comorbid risk factors	0.84% (95% CI: 0.71-1.01)
2)	Body weight = 200, BMI = 33.3 No other comorbid risk factors	1.55% (95% CI: 1.25-1.93)
3)	Body weight = 200, BMI = 33.3 Anemia, Depression Drug Abuse, Hypertension	3.89% (95% CI: 3.00-5.05)
4)	Body weight = 200, BMI = 33.3 Anemia, Depression Drug Abuse. Hypertension Hypothyroidism	4.18% (95% CI: 2.13-8.03)

[8] Available at: http://riskcalc.aaos.org/calculator.php

[9] Given her history of alcohol-related legal difficulties, I suspect that Ms. Axline consumed more alcohol that she admitted to in her testimony and medical interviews. However, because the available evidence does not support my suspicion, I have not included Alcohol Abuse among her comorbid risk factors.

It can be seen that compared to an otherwise similar person without comorbid risk factors, a level of obesity comparable to Ms. Axline' would alone nearly double the relative risk of PJI. With the inclusion of Ms. Axline's other comorbidities the relative risk of PJI would increase nearly five-fold.

Thus, it is not just the individual risk factors, but their combinations that explain in this case a nearly five-fold increase of infection risk. Likewise, they explain the variability of risk in other patients. Such large risk variations are not related to or explained by the various possible sources of bacteria: they are determined in each case by the patient's underlying condition and comorbid factors.

F. Bair Hugger and Prosthetic Joint Infections

20. In my previous reports and testimony, I opined that there was insufficient evidence that use of Bair Hugger caused increased rates of PJI. I discussed the McGovern study (39), on which Dr. Jarvis now relies, but which is flawed by systematic bias and confounders that were ignored in the analysis. In addition, the surgical infection data presented in McGovern were truncated, internally inconsistent, and incorrectly tabulated. For such reasons, I concluded that that study lacked validity and could not be relied upon as evidence of a significant association.

21. A recent study by Dr. Mike Reed, senior author of the McGovern study, provides further insight into the limitations of that original study. That recent report, Jeans et al (40), describes the beneficial effects of pre-operative screening and decolonization for methicillin sensitive Staphylococcal aureus (MSSA) in TJA patients at the Wansbeck General Hospital. The results confirm Reed's earlier, less formal report of the benefits of MSSA screening (37). This study confirms that adoption of MSSA screening almost exclusively for patients using the non-BH warmer confounded the results of the McGovern study. The Jeans study also demonstrates two other failings of the McGovern study.

21a) The McGovern study began in July 2008 because, according to Dr. Reed's deposition, surveillance data were incomplete prior to that date [Reed depo p. 63-4]. However, the Jeans report states that there were "complete data available from prior to screening programme (1st January 2007 to 31st December 2009)". Thus, the Jeans study seemingly contradicts that testimony and provides evidence that the dataset used in the McGovern study was arbitrarily truncated.

21b) An important limitation of the McGovern study was that its analyses were only univariate, thus the effects of confounders were ignored. The Jeans study employed multivariate analyses, indicating that Reed and colleagues recognized the greater statistical meaningfulness of studies that simultaneously consider the impacts of confounding factors.

Thus it is my opinion that there is now even greater reason to discount the McGovern study as biased and unreliable.

22. The lack of probative value of the McGovern study can be seen from another perspective. Despite a burgeoning literature on arthroplasty and PJIs, McGovern remains the only study that purports to present clinical evidence that Bair Hugger is associated with an increased risk of PJI. The significance of the fact that the study is so isolated and unconfirmed is made more obvious by consideration of the actual numbers of published PJI studies. The following graph (adapted from (8)) illustrates the increasing number of PJI studies and reports published between 1982 and 2014.

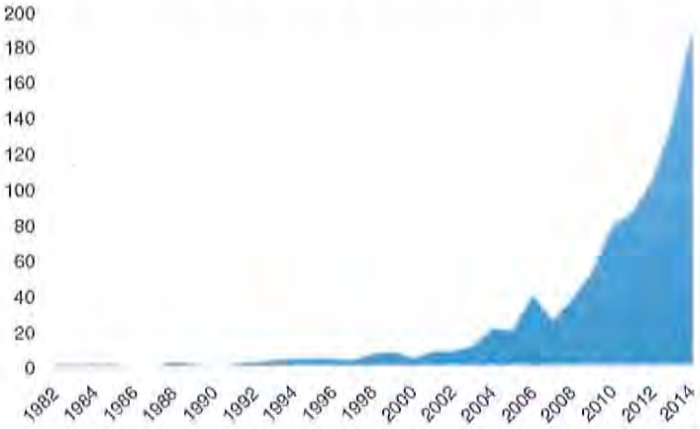

Fig.5.2 Increasing number of PubMed publications that study PJI each year

adapted from (8)

23. To determine the more recent history of such studies, I accessed PubMed to determine the total numbers of PJI reports published since 2014 (including the first seven months of 2018): [10]

Year	# of PJI Publications
2014	279
2015	326
2016	374
2017	430
01/18-07/18	308

Thus, despite increasing concerns about the causes of PJI and the accumulation of more than 2100 PJI publications, the McGovern study remains unconfirmed as the only clinical report claiming that use of Bair Hugger is associated with increased rates of PJI.

24. The Jarvis report also alludes to "various case reports" that support his opinion that "Bair Hugger significantly increases risks of PJI," but those case reports are not identified. Moreover, case reports cannot provide evidence of "increased risks of PJI" due to Bair Hugger because they do not provide the sorts of quantitative data necessary to perform such risk calculations. Thus the Jarvis statement is logically inconsistent and statistically without meaning.

[10] PubMed is medical literature database system maintained by the US National Library of Medicine.

25. Accordingly, it is my opinion that there is no valid evidence that use of Bair Hugger increases the risk of PJIs.

G. Report of Dr. Jarvis

26. In his report, Dr. Jarvis states that "the determinative issue is therefore the most likely ***mechanistic source*** of the bacteria that inoculated the joint". His report goes on to consider a number of possible "mechanistic sources" of bacteria. However, it is not correct to assert that source of bacteria was necessarily the determinative factor in this case. His methodological approach ignores other relevant and well-documented factors that are proven to directly contribute to the risk of surgical infections.

27. Dr. Jarvis failed to consider a number of factors other than "mechanistic sources" of bacteria that are of proven relevance to the development of surgical infections (41-44). Following are three examples of causes of infection that are not "mechanistic sources" of inoculation.

27a) Perioperative Hypothermia: One example is maintenance of perioperative normothermia to prevent hypothermia. There is sufficient evidence that warming surgical patients reduces rates of SSI. And, as discussed below, there is also evidence that maintaining normothermia significantly reduces the risks of other important surgical complications. For such reasons, use of perioperative warming has become a standard of current surgical care, recommended by CDC (42) and WHO (43). The ability of maintaining normothermia to prevent surgical infections is related to the adverse effects of hypothermia on blood flow (vasoconstriction) and decreased tissue perfusion, impaired tissue healing, and suppressed immune function (43). I am not aware of any evidence that patient hypothermia is a ***mechanistic source*** of bacteria, yet it can directly increase the risks and rates of surgical infection.

It is notable that Ms. Axline was mildly hypothermic (i.e., <36˚C) throughout her surgery on 4/21/09.

27b) Tissue Oxygenation and Prophylactic Antibiotic Dosing: In my earlier reports, I considered other intraoperative factors that directly contribute to the risks of PJI, but which are not examples of ***mechanistic sources*** of infection. For example, I considered inadequate tissue oxygenation and inadequate dosing of prophylactic antibiotics. My purpose was to indicate that such factors can and do directly lead to increased risks of infection in surgical patients without being ***mechanistic sources***.

Decreased tissue oxygenation is one of the mechanisms proposed to explain increased rates of surgical infections in patients with diabetes, anemia, obesity and cardiovascular disease. Increased rates of surgical infection in obese patients may also be due to inadequate prophylactic antibiotic dosing, a result of obesity-related effects on the pharmacokinetics of antibiotics. I am not aware of any evidence that

inadequate tissue oxygenation or prophylactic dosing is a ***mechanistic source*** of bacteria, yet they can directly increase the risks and rates of surgical infection.

It is notable that Ms. Axline was obese and that she suffered longstanding iron deficiency and anemia.

27c) Immune System Dysfunction: It is generally understood that suppression of normal immune function predisposes to infections including those following surgery. And, as discussed above, both opioid use and hypothyroidism have been shown to disrupt and suppress immune function. Likewise, immunosuppressed AIDS patients are at increased risk of post-operative bacterial infections. However, such abnormalities of the immune system, whether due to opioids, thyroid dysfunction or AIDS, are not ***mechanistic sources*** of bacteria, although they are important risk factors for infection.

It is notable that Ms. Axline had a long history of hypothyroidism, was an opioid abuser, and took large amounts of opioids immediately prior to her surgery.

28. Thus, it is my opinion that Dr. Jarvis ignored important factors that have been repeatedly shown to directly contribute to surgical site infections, choosing to focus solely on "***mechanistic sources***". It is of particular relevance that he ignored the importance of obesity, iron deficiency and anemia, hypothyroidism, and opioid abuse to the development of Ms. Axline's post-operative infection.

29. In addition, Dr. Jarvis considered only intraoperative sources of infection, focusing on OR procedures and staff behaviors during Ms. Axline's surgery. As I have previously discussed, it is well recognized that PJI can result from post-operative exposures including bacterial entry at the surgical site or blood-borne bacterial seeding. It is my opinion that Dr. Jarvis had no objective basis for concluding that Ms. Axline's infection was specifically due to intraoperative inoculation of the wound.

30. With regards to his narrow focus on intraoperative sources of infection, Dr. Jarvis opined that the "surgical procedures and techniques could be ruled out as a likely cause". That statement is not consistent with the opinions of Dr. Reed, the senior author of the McGovern study, and it is not consistent with the opinions of Dr. Lombardi, Ms. Axline's orthopedic surgeon.

30a) Dr. Reed wrote in 2015 that: "Contaminants may arise from the patient' skin, from the surgical personnel or from the surgical instrumentation itself. It is likely that almost all surgical wounds are contaminated because skin preparation at the time of surgery will only decontaminate the skin surface and bacteria will remain in deeper layers of the skin" (37).

30b) Dr. Lombardi testified in a similar manner:

Q. Did you change the scalpel blade after the initial incision?

A. I always have used one scalpel to make the incision, and then go to a second scalpel for the remainder of the operation.
Q. Why is that?
A. Theoretical risk of infection. We feel -- every one of us in the room is contaminated. Our skin is contaminated. It carries flora on it. And we know that by taking that knife and striking it through the skin, it's going to have some bacterial content on it. [Lombardi depo p.64]

31. Dr. Jarvis also concluded that because of the skin preparation performed at the time of surgery, he could rule out infection attributable to Ms. Axline's own flora. However, there is no scientific basis for that opinion. For example, Dr. Jarvis actually acknowledged that the skin preparation would not fully eliminate all skin flora. Likewise, in his testimony, Dr. Lombardi affirmed that skin preparation did not actually sterilize the skin:

Q. And did the skin prep completely eliminate all bacteria from the patient's skin?
A. I think it's common knowledge that it does not. [Lombardi depo p.64]

It is also well known that "microorganisms colonizing the skin not only reside on the skin surface but are also found to inhabit hair follicles and lower skin depths" (45). It is estimated that more than 25% of skin bacteria, particularly including Staphylococcus, are found beneath the superficial cells of the stratum corneum (i.e., the outer layer of skin) and in the hair follicles where they are protected from the bactericidal effects of surgical skin preps (45-48).

32. Furthermore, Dr. Jarvis concluded "based on my review of the medical records" that staff followed appropriate standards of care and that there was "no evidence" of any break in the sterile field. However, there is evidence that violations of OR antisepsis protocols occur with surprising frequency, even with well-trained university-based OR staff. For example, Dr. Lombardi agreed that despite his own exemplary record, he sometimes discovered nicks or holes in his otherwise sterile gloves

Q. Are there -- and have there been occasions where at the end of the surgery, when you're taking off your gloves, you discover that there have been two nicks that you didn't realize during the surgery?
A. I've done 30,000 operations. Yes. [Lombardi depo p.65-6]

In addition, I previously discussed the findings from a Swiss university hospital that monitored compliance with OR antisepsis protocols by assigning "experienced" nurses to observe the behavior of OR staff during surgery (49). In that study, one or more protocol violations occurred in 66.2% of cases; three or more violations occurred in 25.1%. One or more violations was associated with a more than doubling of the surgical infection rate (OR: 2.02, 95% CI: 1.05-3.88, $p = 0.04$). The occurrence of such protocol violations does not necessarily imply deviations from standards of care:

"standards of care" do not imply perfection.[11] It seems that strict adherence to intraoperative antisepsis protocols, even in university hospitals, is the exception.

Thus it is my opinion that Dr. Jarvis could not rule out "surgical procedures and techniques" as a "likely cause" of Ms. Axline's infection simply because, based on his review of the written records, "the standard of care was employed throughout his surgery and hospital stay."

33. Also in his report, Dr. Jarvis states that "a relative risk of 2.0 in and of itself shows that the device or drug at issue is the most likely cause of the disease". That statement is fundamentally wrong. While it is correct to say that a relative risk ≥ 2 indicates that the specific association in the specific context is more likely than not true (i.e., not due to chance), it does not mean that the association is causal. In my previous reports, I provided several examples to illustrate the error of Dr. Jarvis' statement. I also provided an example to illustrate that each of multiple risk factors could simultaneously have relative risks ≥ 2.0. Thus, reliance on the RR alone, "in and of itself," could not differentiate between alternative potential causes of infection.

34. Dr. Jarvis relied on a relative risk value derived from the McGovern study to conclude causation. Over and beyond that study's methodological flaws, that relative risk value was determined using only a univariate analysis. Because such analyses ignore other potential causes and confounders, reliance solely on that calculated value also ignored other potential causes and confounders. In fact, the McGovern study did not evaluate other potential causes. In addition, the study findings have not been replicated in a valid study.

35. Thus it is my opinion that Dr. Jarvis could not rely solely on the McGovern study and its calculated relative risk as the basis for concluding that Bair Hugger causes infections.

36. In addition to the McGovern study, Dr. Jarvis relied on a combination of particle-related studies to support his opinion that Bair Hugger caused Ms. Axline's infection:

> "The McGovern study and/or Dr. Elghobashi's CFD model paired with the Stocks and Darouiche studies each independently confirm that the Bair Hugger is the most likely cause of Ms. Axline's PJI." [Report p.12]

I have earlier described the clinical component of the McGovern study and the reasons that it "does not independently confirm" that Bair Hugger caused her infection. A second component of that study involved use of "neutrally buoyant detergent bubbles" to visualize airflow patterns in an OR during simulated surgery, comparing two different warming devices, Bair Hugger vs. a device manufactured by Augustine Temperature

[11] "Medical Definition of Standard of care: ... the level at which the average, prudent provider in a given community would practice. It is how similarly qualified practitioners would have managed the patient's care under the same or similar circumstances."
https://www.medicinenet.com/script/main/art.asp?articlekey=33263

Management. The bubbles were 4 mm (4000 µm) in diameter. The study reported that more bubbles were visualized over the "surgical site" when Bair Hugger was used.

The bubble component of the McGovern study did not consider bacteria and it did not consider infections. As discussed below, it also did not consider particles comparable in size or composition to those of the Elghobashi, Stocks and Darouiche studies. Accordingly, it does not "independently confirm" that Bair Hugger is the most likely cause of Ms. Axline's infection and when "paired with" the Elghobashi and/or Stocks and Darouiche studies, it does not confirm that Bair Hugger is the most likely cause of Ms. Axline's infection. An additional source of concern is the possibility of bias introduced by the fact that this component of the McGovern study was directed by Mr. Albrecht, then an employee of Augustine Temperature Management.

Following is a discussion of the Elghobashi, Stocks and Darouiche studies, as well as several other "particle-related" studies, indicating that such studies also do not confirm, "independently" or in conjunction, that Bair Hugger caused Ms. Axline's infection.

36a) The Elghobashi study (50) is a computer simulation ("large eddy simulation") of hypothetical exposures in an imaginary OR ("The CAD model simulated a realistic OR … [it] also includes several items that are usually present in a real OR"). The model was used to calculate the probable distributions of shed skin cells placed on the floor of an OR that might reach "the surgical site … 4 imaginary boxes of interest"). The study did not include any actual patients or surgeries, it did not consider actual particles, and it did not consider PJIs. The hypothetical particles considered in the study had aerodynamic diameters of exactly 10 µm, although the authors noted that particles of theoretical concern actually range from 4 to 20 µm. (By contrast, the McGovern bubble study used 4000 µm "particles", 200- to 1000-fold greater than the range of "theoretical concern".) In concluding, the authors agreed that the study was not based on "detailed experimental measurements … in an OR during a clinical trial" and that there was need for real world studies to validate their findings.

Accordingly, the relevance of this not-yet-validated, hypothetical simulation to the actual infection suffered by Ms. Axline is uncertain and not obvious.

36b) The Stocks study (51) involved simultaneous collection of 10-minute air samples during orthopedic procedures and their analysis for airborne particles (6 bins categorized by diameter) and colony forming units (CFUs, a measure of bacteria). The key concern was the relationship between particle number and CFU number. The analyses included "bivariate" regression and multivariate regression.

The bivariate regressions indicated significant positive relationships between CFU number and particle number for 5-9.9 µm and ≥10 µm particles, but not for smaller particles.[12] While significant, the effect of the 5-9.9 µm particles was less than 5%

[12] The analyses actually considered the square root transformation of the CFU count.

that of the ≥10 µm particles. Multivariate analyses indicate that only the ≥10 µm particles were positively and significantly related to CFU counts. In a model that included both 5-9.9 µm and ≥10 µm particles, the parameter for 5-9.9 µm particles was high significant and negative (p = 0.001).[13] These results indicate that the apparent positive association of CFU and 5-9.9 µm particles was due to confounding. Moreover, they suggest a possible significant negative relationship between the number of 5-9.9 µm particles and CFU count. In other words, the multivariate analyses suggest that increased 5-9.9 µm particle counts might protect against bacterial contamination. (Stocks did not consider particles ≥4000 µm (or 4mm), the size of the McGovern bubbles).

The relevance of Stocks to either general questions about Bair Hugger or specific questions about Ms. Axline is not obvious. First, Stocks did not study Bair Hugger and none of the study patients developed "clinical signs or symptoms of infection". Second, as detailed below, I am not aware of any studies documenting increased numbers of airborne particles ≥10 µm (other than McGovern's 4000 µm detergent bubbles) as a result of Bair Hugger.

36b$_1$) Legg et al (52) tested Bair Hugger in an actual OR in which a volunteer was positioned on an operating table and a surgeon simulated TKA surgery, but no nurses were employed. The numbers of particles, according to three bins (0.3 µm, 0.5 µm, and 5.0 µm), were counted over the "surgical site" five times during the mock procedure. Compared to no warming, particles counts were significantly increased with Bair Hugger, but 99.7% of particles were <5.0 µm. No data were determined for particles >5 µm. (Note that Stocks reported that particles of the size counted in this study were not association with CFU counts).

36b$_2$) Legg and Hamer (53) replicated the experimental conditions of their prior study using artificial smoke ("glycerol tracer particles") to visualize air flows during simulated surgery using Bair Hugger. However, the particles they used were 0.3 µm in diameter. No information was provided about larger particles. (Note that Stocks reported that particles of the size used in this study were not association with CFU counts).

36b$_3$) McGovern et al [McGovern depo exhibit 6, 01/04/17][14] described an experiment in an actual OR in which a volunteer was positioned on an operating table and surgery was simulated. The numbers of airborne particles, according to three bins (0.3 µm, 0.5 µm, and 5.0 µm), were counted over the "surgical site" during use of Bair Hugger. The study found "no notable increase in … ambient particle count when a forced air warming device is being used."

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[13] Regression parameters indicate the direction and magnitude of the effect of each specific variable on the outcome of concern.

[14] McGovern PD et al: Do forced air warming devices increase factorial contamination of operative field? – Simulated experiment analysis. McGovern depo exhibit 6: 01/04/17 and 01/05/17.

In summary, the Stocks study did not consider Bair Hugger and its results are not relevant to the size of particles that have been associated with use of Bair Hugger. Thus, the Stocks findings seem unrelated to the documented effects of Bair Hugger and they are not directly relevant to the infection suffered by Ms. Axline.

36c) Darouiche et al (54) performed a random control trial of an "air barrier system" to reduce particle counts over the surgical site during various procedures. Half of the patients underwent THA; the others had spinal or vascular procedures. Bair Hugger was not used. Numbers of particles (0.3 µm, 0.5 µm, 1 µm, 5 µm and ≥10 µm) and numbers of CFU were measured during the first 100 minutes of each case. Use of the barrier significantly reduced the number of total particulates and CFU, but results were not provided according to particle size. CFU count was significantly associated with deep, but not with incisional infections; that association was not reported by particle size. A series of sub-analyses considered relationships between particle number grouped by size, CFU number, and specific risk factors: In the controls (i.e., no barrier), there were no significant associations between CFU count and particles ≥10 µm. (By contrast, Stocks reported a significant association between CFU count and particles ≥10 µm, while the McGovern bubble study used only "particles" ≥4000 µm.)

Because this study did not consider Bair Hugger and because it did not report significant associations between CFU count and particles ≥10 µm, it is not obvious that Darouiche provides support for the Stocks study. Likewise, it is not obvious that Darouiche is directly relevant to the infection suffered by Ms. Axline.

The differences in the sizes of particles considered in the above studies are not merely analytical distinctions: they have real world importance. As emphasized by Elghobashi, and fist described by Noble in 1964 (55), particles that carry bacteria are in the range of 4 to 20 µm. Thus, the particles that have been associated with use of Bair Hugger are too small to carry bacteria.

`37. Thus it is my opinion that Dr. Jarvis could not rely on the bubble component of the McGovern study and/or the Elghobashi, Stocks and Darouiche studies as the basis for concluding that Bair Hugger causes infections.

H. Hypothermia and Other Surgical Complications

38. The discussion above largely focused on risk factors, including hypothermia, that have been associated with increased risk of surgical infections. It might wrongly be inferred that the reason for using Bair Hugger is solely to prevent infections. To the contrary, there is evidence that perioperative hypothermia is associated with a variety of important surgical complications other than infection. This was well summarized in a 2013 report by Leijtens et al (56):

> "Inadvertent hypothermia is an important complication of major surgery. Even mild peri-operative hypothermia can cause a variety of adverse effects (57), such

> as: morbid myocardial events (58), increased risk of surgical peri-prosthetic infections, increased duration of hospitalization (59-61), intra-operative blood loss (62;63) and prolonged postanesthetic recovery (59). These effects can be considerable, a decrease of 1.9 °C in core temperature triples the relative risk of surgical peri-prosthetic infection and increases the duration of hospitalization by 20% (59;61)."

It should also be noted that during his deposition, Dr. Narcelles (Ms. Axline's anesthesiologist) testified similarly about the benefits of perioperative warming. He said that he had warmed her during surgery to "mitigate heat loss" and, when then asked why he wanted to mitigate heat loss he said:

> A. Because when -- because general anesthesia, spinal anesthesia for that matter, has a tendency to make people get cooler, plus being in an operating room that's lower than body temperature will also cause people to become cooler as well. And when people get cool or hypothermic, that can cause a variety of medical issues, which are not good for the patient. So we use the Bair Hugger to prevent that loss.
> Q. Q. Okay. And what are those variety of medical issues that can occur with hypothermia?
> A. Let me see, the most common things are we worry about heart problems. So you can see arrhythmias, like atrial fibrillation, bradycardia, up to ventricular tachycardia if they get cold enough. There's also an increase in morbid cardiac events. So you see things like cardiac ischemia or chest pain or like lack of blood flow to the heart or actual heart attacks or actually cardiac arrests. Those are -- all happen more frequently if a patient is allowed to be cold.
> In terms of bleeding, when patients are hypothermic, there is a coagulopathy. The blood doesn't coagulate as well because of inhibition of the platelets ... so you tend to lose more blood... When people are hypothermic, it can cause -- it can make them more susceptible to surgical infection.
> The other thing we worry about is there's a -- the body when they are cold -- it's cold, doesn't metabolize medications as much ... so if they are allowed to be cold, that medication doesn't necessarily wear off by the end of the operation.
> ...
> Q. Okay. Any other medical issues that you are aware of that relate to hypothermia?
> A. Well, there are a lot of them ... [Narcelles depo, p.72-74]

For such reasons, use of perioperative warming has become a standard of current surgical care, recommended by CDC (42) and WHO (43).

I. Summary

39. Following is a list of my opinions, all to a reasonable degree of medical and scientific certainty.

39a) There is no valid evidence that use of Bair Hugger increases the risk of PJIs. Accordingly, there is no basis to conclude that use of Bair Hugger "is the most likely cause of Ms. Axline's PJI."

39b) There is no objective basis for concluding that Ms. Axline's infection was due to intraoperative inoculation of the wound.

39c) Ms. Axline's obesity was a risk factor that directly contributed to her development of PJI.

39d) Ms. Axline's use and abuse of opioids was a risk factor that directly contributed to her development of PJI.

39e) Ms. Axline's iron deficiency was a risk factor that directly contributed to her development of PJI.

39f) Ms. Axline's hypothyroidism was a risk factor that directly contributed to her development of PJI.

39g) Ms. Axline's hypertension and hypercholesterolemia were risk factors that directly contributed to her development of PJI.

40. I reserve the right to amend my report and opinions should further information become available.

I declare under penalty of perjury that the foregoing is true and correct

Jonathan Borak, MD, FACP, FACOEM

Reference List

(1) Centers for Disease Control and Prevention (CDC). Growth Chart Training: Calculating BMI Using the English System (https://www.cdc.gov/nccdphp/dnpao/growthcharts/training/bmiage/page5_2.html). Atlanta: U.S. Department of Health & Human Services, Centers for Disease Control and Prevention (CDC); 2014.

(2) Jonklaas J, Bianco AC, Bauer AJ, Burman KD, Cappola AR, Celi FS et al. Guidelines for the treatment of hypothyroidism: prepared by the american thyroid association task force on thyroid hormone replacement. Thyroid 2014; 24:1670-1751.

(3) McAninch EA, Rajan KB, Miller CH, Bianco AC. Systemic Thyroid Hormone Status During Levothyroxine Therapy In Hypothyroidism: A Systematic Review and Meta-Analysis. J Clin Endocrinol Metab 2018; still in print.

(4) Haverkamp D, Klinkenbijl MN, Somford MP, Albers GH, van der Vis HM. Obesity in total hip arthroplasty--does it really matter? A meta-analysis. Acta Orthop 2011; 82:417-422.

(5) Liu W, Wahafu T, Cheng M, Cheng T, Zhang Y, Zhang X. The influence of obesity on primary total hip arthroplasty outcomes: A meta-analysis of prospective cohort studies. Orthop Traumatol Surg Res 2015; 101:289-296.

(6) Kerkhoffs GM, Servien E, Dunn W, Dahm D, Bramer JA, Haverkamp D. The influence of obesity on the complication rate and outcome of total knee arthroplasty: a meta-analysis and systematic literature review. J Bone Joint Surg Am 2012; 94:1839-1844.

(7) Kunutsor SK, Whitehouse MR, Blom AW, Beswick AD. Patient-related risk factors for periprosthetic joint infection after total joint arthroplasty: A systematic review and meta-analysis. PloS One 2016; 11(3):e0150866.

(8) Tan TL, Kheir MM, Chen AF. Who is at Risk for Periprosthetic Joint Infection? In: Kendoff D, Morgan-Jones R, Haddad FS, editors. Periprosthetic Joint Infections. Changing Paradigms. Swizerland: Springer; 2016. 61-75.

(9) Tan TL, Maltenfort MG, Chen AF, Shahi A, Higuera CA, Siqueira M et al. Development and evaluation of a preoperative risk calculator for periprosthetic joint infection following total joint arthroplasty. J Bone Joint Surg Am 2018; 100:777-785.

(10) Bozic KJ, Lau E, Kurtz S, Ong K, Rubash H, Vail TP et al. Patient-related risk factors for periprosthetic joint infection and postoperative mortality following total hip arthroplasty in Medicare patients. J Bone Joint Surg Am 2012; 94:794-800.

(11) Bozic KJ, Lau E, Kurtz S, Ong K, Berry DJ. Patient-related risk factors for postoperative mortality and periprosthetic joint infection in medicare patients undergoing TKA. Clin Orthop Relat Res 2012; 470:130-137.

(12) Lenguerrand E, Whitehouse MR, Beswick AD, Kunutsor SK, Burston B, Porter M et al. Risk factors associated with revision for prosthetic joint infection after hip replacement: a prospective observational cohort study. Lancet Infect Dis 2018; still in print.

(13) Bell KL, Shohat N, Goswami K, Tan TL, Kalbian I, Parvizi J. Preoperative opioids increase the risk of periprosthetic joint infection after total joint arthroplasty. J Arthroplasty 2018; still in print.

(14) Goodnough LT, Maniatis A, Earnshaw P, Benoni G, Beris P, Bisbe E et al. Detection, evaluation, and management of preoperative anaemia in the elective orthopaedic surgical patient: NATA guidelines. Br J Anaesth 2011; 106:13-22.

(15) Myers E, O'Grady P, Dolan AM. The influence of preclinical anaemia on outcome following total hip replacement. Arch Orthop Trauma Surg 2004; 124:699-701.

(16) Conlon NP, Bale EP, Herbison GP, McCarroll M. Postoperative anemia and quality of life after primary hip arthroplasty in patients over 65 years old. Anesth Analg 2008; 106:1056-1061.

(17) Greenky M, Gandhi K, Pulido L, Restrepo C, Parvizi J. Preoperative anemia in total joint arthroplasty: is it associated with periprosthetic joint infection? Clin Orthop Relat Res 2012; 470:2695-2701.

(18) De Vito P, Incerpi S, Pedersen JZ, Luly P, Davis FB, Davis PJ. Thyroid hormones as modulators of immune activities at the cellular level. Thyroid 2011; 21:879-890.

(19) Schoenfeld PS, Myers JW, Myers L, LaRocque JC. Suppression of cell-mediated immunity in hypothyroidism. South Med J 1995; 88:347-349.

(20) De Vito P, Balducci V, Leone S, Percario Z, Mangino G, Davis PJ et al. Nongenomic effects of thyroid hormones on the immune system cells: New targets, old players. Steroids 2012; 77:988-995.

(21) Grunfeld R, Kunselman A, Bustillo J, Juliano PJ. Wound complications in thyroxine-supplemented patients following foot and ankle surgery. Foot Ankle Int 2011; 32:38-46.

(22) Tan TL, Rajeswaran H, Haddad S, Shahi A, Parvizi J. Increased risk of periprosthetic joint infections in patients with hypothyroidism undergoing total joint arthroplasty. J Arthroplasty 2016; 31:868-871.

(23) Buller LT, Rosas S, Sabeh KG, Roche MW, McLawhorn AS, Barsoum WK. Hypothyroidism Increases 90-Day Complications and Costs Following Primary Total Knee Arthroplasty. J Arthroplasty 2018; 33:1003-1007.

(24) Althoff A, Cancienne JM, Cooper MT, Werner BC. Patient-Related Risk Factors for Periprosthetic Ankle Joint Infection: An Analysis of 6977 Total Ankle Arthroplasties. J Foot Ankle Surg 2018; 57:269-272.

(25) Sacerdote P. Opioids and the immune system. Palliat Med 2006; 20 (suppl 1):s9-s15.

(26) Sacerdote P. Opioid-induced immunosuppression. Curr Opin Support Palliat Care 2008; 2:14-18.

(27) Odunayo A, Dodam JR, Kerl ME, DeClue AE. Immunomodulatory effects of opioids. J Vet Emerg Crit Care (San Antonio) 2010; 20:376-385.

(28) Menendez ME, Ring D, Bateman BT. Preoperative opioid misuse is associated with increased morbidity and mortality after elective orthopaedic surgery. Clin Orthop Relat Res 2015; 473:2402-2412.

(29) Cozowicz C, Olson A, Poeran J, Morwald EE, Zubizarreta N, Girardi FP et al. Opioid prescription levels and postoperative outcomes in orthopedic surgery. Pain 2017; 158:2422-2430.

(30) Cancienne JM, Patel KJ, Browne JA, Werner BC. Narcotic use and total knee arthroplasty. J Arthroplasty 2018; 33:113-118.

(31) Szabo G, Saha B. Alcohol's effect on host defense. Alcohol Res 2015; 37:159-170.

(32) Barr T, Helms C, Grant K, Messaoudi I. Opposing effects of alcohol on the immune system. Prog Neuropsychopharmacol Biol Psychiatry 2016; 65:242-251.

(33) Pasala S, Barr T, Messaoudi I. Impact of alcohol abuse on the adaptive immune system. Alcohol Res 2015; 37:185-197.

(34) Dguzeh U, Haddad NC, Smith KTS, Johnson JO, Doye AA, Gwathmey JK et al. Alcoholism: A multi-systemic cellular insult to organs. Int J Environ Res Public Health 2018; 15.

(35) Best MJ, Buller LT, Gosthe RG, Klika AK, Barsoum WK. Alcohol Misuse is an Independent Risk Factor for Poorer Postoperative Outcomes Following Primary Total Hip and Total Knee Arthroplasty. J Arthroplasty 2015; 30:1293-1298.

(36) Kong L, Cao J, Zhang Y, Ding W, Shen Y. Risk factors for periprosthetic joint infection following primary total hip or knee arthroplasty: a meta-analysis. Int Wound J 2017; 14:529-536.

(37) Refaie R, Jameson S, Reed M. Prevention of periprosthetic joint infection. J Trauma Ortho 2015; 3:50-52.

(38) Birgand G, Toupet G, Rukly S, Antoniotti G, Deschamps MN, Lepelletier D et al. Air contamination for predicting wound contamination in clean surgery: A large multicenter study. Am J Infect Control 2015; 43:516-521.

(39) McGovern PD, Albrecht M, Belani KG, Nachtsheim C, Partington PF, Carluke I et al. Forced-air warming and ultra-clean ventilation do not mix: an investigation of theatre ventilation, patient warming and joint replacement infection in orthopaedics. J Bone Joint Surg Br 2011; 93:1537-1544.

(40) Jeans E, Holleyman R, Tate D, Reed M, Malviya A. Methicillin sensitive staphylococcus aureus screening and decolonisation in elective hip and knee arthroplasty. J Infect 2018; still in print.

(41) Anderson DJ, Podgorny K, Berrios-Torres SL, Bratzler DW, Dellinger EP, Greene L et al. Strategies to prevent surgical site infections in acute care hospitals: 2014 update. Infect Control Hosp Epidemiol 2014; 35 (suppl 2):S66-S88.

(42) Berrios-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR et al. Centers for Disease Control and Prevention guideline for the prevention of surgical site infection, 2017. JAMA Surg 2017; 152:784-791.

(43) Allegranzi B, Zayed B, Bischoff P, Kubilay NZ, de Jonge S, de Vries F et al. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. Lancet Infect Dis 2016; 16:e288-e303.

(44) Dellinger EP, Hausmann SM, Bratzler DW, Johnson RM, Daniel DM, Bunt KM et al. Hospitals collaborate to decrease surgical site infections. Am J Surg 2005; 190:9-15.

(45) Karpanen TJ, Worthington T, Conway BR, Hilton AC, Elliott TSJ, Lambert PA. Penetration of chlorhexidine into human skin. Antimicrob Agents Chemother 2008; 52:3633-3636.

(46) Montes LF, Wilborn WH. Anatomical location of normal skin flora. Arch Dermatol 1970; 101:145-159.

(47) Montes LF, Wilborn WH. Location of bacterial skin flora. Br J Dermatol 1969; 81 (suppl 1):23-26.

(48) Lange-Asschenfeldt B, Marenbach D, Lang C, Patzelt A, Ulrich M, et al. Distribution of bacteria in the epidermal layers and hair follicles of the human skin. Skin Pharmacol Physiol 2011; 24:305-311.

(49) Beldi G, Bisch-Knaden S, Banz V, Muhlemann K, Candinas D. Impact of intraoperative behavior on surgical site infections. Am J Surg 2009; 198:157-162.

(50) He X, Karra S, Pakseresht P, Apte SV, Elgobashi S. Effect of heated-air blanket on the dispersion of squames in an operating room. Int J Numer Meth Biomed Engeng 2018; 34:e2960.

(51) Stocks GW, Self SD, Thompson B, Adame XA, O'Connor DP. Predicting bacterial populations based on airborne particulates: A study performed in nonlaminar flow operating rooms during joint arthroplasty surgery. Am J Infect Control 2010; 38:199-204.

(52) Legg AJ, Cannon T, Hamer AJ. Do forced air patient-warming devices disrupt unidirectional downward airflow? J Bone Joint Surg Br 2012; 94:254-256.

(53) Legg AJ, Hamer AJ. Forced-air patient warming blankets disrupt unidirectional airflow. Bone Joint J 2013; 95-B:407-410.

(54) Darouiche RO, Green DM, Harrington MA, Ehni BL, Kougias P, Bechara CF et al. Association of Airborne Microorganisms in the Operating Room With Implant Infections: A Randomized Controlled Trial. Infect Control Hosp Epidemiol 2017; 38:3-10.

(55) Noble WC, Lidwell OM, Kingston D. The size distribution of airborne particles carrying micro-organisms. J Hyg (London) 1963; 61:385-391.

(56) Leijtens B, Koeter M, Kremers K, Koeter S. High incidence of postoperative hypothermia in total knee and total hip arthroplasty: a prospective observational study. J Arthroplasty 2013; 28:895-898.

(57) Reynolds L, Beckmann J, Kurz A. Perioperative complications of hypothermia. Best Pract Res Clin Anaesthesiol 2008; 22:645-657.

(58) Frank SM, Fleisher LA, Breslow MJ, Higgins MS, Olson KF, Kelly S et al. Perioperative maintenance of normothermia reduces the incidence of morbid cardiac events. A randomized clinical trial. J Am Med Assoc 1997; 277:1127-1134.

(59) Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. NEJM 1996; 334:1209-1215.

(60) Melling AC, Ali B, Scott EM, Leaper DJ. Effects of preoperative warming on the incidence of wound infection after clean surgery: a randomised controlled trial. Lancet 2001; 358:876-880.

(61) Kurz A. Thermal care in the perioperative period. Best Pract Res Clin Anaesthesiol 2008; 22:39-62.

(62) Schmied H, Kurz A, Sessler DI, Kozek S, Reiter A. Mild hypothermia increases blood loss and transfusion requirements during total hip arthroplasty. Lancet 1996; 347:289-292.

(63) Rajagopalan S, Mascha E, Na J, Sessler DI. The effects of mild perioperative hypothermia on blood loss and transfusion requirement. Anesthesiology 2008; 108:71-77.

BORAK BAIR HUGGER REFERENCE LIST

1. (2012). HAI Watchdog Awards 2011. *Operating Theatre J*, 10-11.
   Ref ID: 36270

2. Abdallah,D.Y., Jadaan,M.M. & McCabe,J.P. (2013). Body mass index and risk of surgical site infection following spine surgery: a meta-analysis. *Eur Spine J*, 22: 2800-2809.
   Ref ID: 36520

3. Adams,A.L., Paxton,E.W., Wang,J.Q., Johnson,E.S., Bayliss,E.A., Ferrara,A., Nakasato,C., Bini,S.A. & Namba,R.S. (2013). Surgical outcomes of total knee replacement according to diabetes status and glycemic control, 2001 to 2009. *J Bone Joint Surg Am*, 95: 481-487.
   Ref ID: 36975

4. Alberg,A.J., Brock,M.V. & Samet,J.M. (2018). Epidemiology of lung cancer: looking to the future. *J Clin Oncol*, 23: 175-185.
   Ref ID: 37013

5. AlBuhairan,B., Hind,D. & Hutchinson,A. (2008). Antibiotic prophylaxis for wound infections in total joint arthroplasty: a systematic review. *J Bone Joint Surg Br*, 90: 915-919.
   Ref ID: 36209

6. Alexander,J.W., Solomkin,J.S. & Edwards,M.J. (2011). Updated recommendations for control of surgical site infections. *Ann Surg*, 253: 1082-1093.
   Ref ID: 36523

7. Allegranzi,B., Zayed,B., Bischoff,P., Kubilay,N.Z., de Jonge,S., de Vries,F., Gomes,S.M. & etal (2016). New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. *Lancet Infect Dis*, 16: e288-e303.
   Ref ID: 36217

8. Allen,D.B., Maguire,J.J., Mahdavian,M., Wicke,C., Marcocci,L., Scheuenstuhl,H., Chang,M., Le,A.X., Hopf,H.W. & Hunt,T.K. (1997). Wound hypoxia and acidosis limit neutrophil bacterial killing mechanisms. *Arch Surg*, 132: 991-996.
   Ref ID: 36554

9. Allen,M.W. & Jacofsky,D.J. (2017). Normothermia in Arthroplasty. *J Arthroplasty*, 32: 2307-2314.
   Ref ID: 36732

BAIR HUGGER REFERENCE LIST
(continued)

10. Althoff,A., Cancienne,J.M., Cooper,M.T. & Werner,B.C. (2018). Patient-Related Risk Factors for Periprosthetic Ankle Joint Infection: An Analysis of 6977 Total Ankle Arthroplasties. *J Foot Ankle Surg*, 57: 269-272.
Ref ID: 36879

11. American Diabetes Association (2018). Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes--2018. *Diabetes Care*, 41 (suppl 1): S13-S27.
Ref ID: 36954

12. Anand,I.S. & Gupta,P. (2018). Anemia and Iron Deficiency in Heart Failure: Current Concepts and Emerging Therapies. *Circulation*, 138: 80-98.
Ref ID: 37005

13. Anderson,D.J., Podgorny,K., Berrios-Torres,S.L., Bratzler,D.W., Dellinger,E.P., Greene,L., Nyquist,A.C., Saiman,L., Yokoe,D.S., Maragakis,L.L. & Kaye,K.S. (2014). Strategies to prevent surgical site infections in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol*, 35 (suppl 2): S66-S88.
Ref ID: 36550

14. Asensio,A., Antolin,F.J., Sanchez-Garcia,J.M., Hidalgo,O., Hernandez-Navarrete,M.J., Bishopberger,C. & et al (2010). Timing of DVT prophylaxis and risk of postoperative knee prosthesis infection. *Orthopedics*, 33: 800.
Ref ID: 36179

15. Atkins,D., Best,D., Briss,P.A., Eccles,M., Falck-Ytter,Y. & Flottorp,S.e.a. (2004). Grading quality of evidence and strength of recommendations. *BMJ*, 328: 1490.
Ref ID: 36577

16. Augustine,S.D. (2017). Forced-air warming discontinued: periprosthetic joint infection rates drop. *Orthop Rev*, 9 (6998): 39-42.
Ref ID: 36335

17. Barbier,F., Ruppe,E., Hernandez,D., Lebeaux,D., Francois,P., Felix,B., Desprez,A., Maiga,A., Woerther,P.L., Gaillard,K., Jeanrot,C., Wolff,M., Schrenzel,J., Andremont,A. & Ruimy,R. (2010). Methicillin-resistant coagulase-negative staphylococci in the community: high homology of SCCmec IVa between Staphylococcus epidermidis and major clones of methicillin-resistant Staphylococcus aureus. *J Infect Dis*, 202: 270-281.
Ref ID: 36606

18. Barr,T., Helms,C., Grant,K. & Messaoudi,I. (2016). Opposing effects of alcohol on the immune system. *Prog Neuropsychopharmacol Biol Psychiatry*, 65: 242-251.
Ref ID: 37045

BAIR HUGGER REFERENCE LIST

(continued)

19. Barrack,R.L., Berend,K.R., Cui,Q., Fehring,T.K., Della Valle,C.J., Gehrke,T., Lombardi,A.V., Jr., Mont,M.A., Parvizi,J. & Springer,B.D. (2013). Cement spacers in periprosthetic joint infection. *Clin Infect Dis*, 57: 328-329.
Ref ID: 36848

20. Bay,L., Kragh,K.N., Eickhardt,S.R., Poulsen,S.S., Gjerdrum,L.M.R., Ghathian,K. & et al (2018). Bacterial aggregates established at the edges of acute epidermal wounds. *Adv Wound Care*, 7: 105-113.
Ref ID: 36988

21. Bearden,D.T. & Rodvold,K.A. (2000). Dosage adjustments for antibacterials in obese patients: applying clinical pharmacokinetics. *Clin Pharmacokinet*, 38: 415-426.
Ref ID: 36524

22. Becker,K., Heilmann,C. & Peters,G. (2014). Coagulase-negative staphylococci. *Clin Microbiol Rev*, 27: 870-926.
Ref ID: 36566

23. Bedard,N.A., Pugely,A.J., Westermann,R.W., Duchman,K.R., Glass,N.A. & Callaghan,J.J. (2017). Opioid use after total knee arthroplasty: trends and risk factors for prolonged use. *J Arthroplasty*, 32: 2390-2394.
Ref ID: 36892

24. Belani,K.G., Albrecht,M., McGovern,P.D., Reed,M. & Nachtsheim,C. (2013). Patient warming excess heat: the effects on orthopedic operating room ventilation performance. *Anesth Analg*, 117: 406-411.
Ref ID: 37003

25. Beldi,G., Bisch-Knaden,S., Banz,V., Muhlemann,K. & Candinas,D. (2009). Impact of intraoperative behavior on surgical site infections. *Am J Surg*, 198: 157-162.
Ref ID: 36530

26. Bell,K.L., Shohat,N., Goswami,K., Tan,T.L., Kalbian,I. & Parvizi,J. (2018). Preoperative opioids increase the risk of periprosthetic joint infection after total joint arthroplasty. *J Arthroplasty*, still in print.
Ref ID: 36967

27. Ben-Ari,A., Chansky,H. & Rozet,I. (2017). Preoperative Opioid Use Is Associated with Early Revision After Total Knee Arthroplasty: A Study of Male Patients Treated in the Veterans Affairs System. *J Bone Joint Surg Am*, 99: 1-9.
Ref ID: 36887

BAIR HUGGER REFERENCE LIST
(continued)

28. Berbari,E.F., Hanssen,A.D., Duffy,M.C., Steckelberg,J.M., Ilstrup,D.M., Harmsen,W.S. & Osmon,D.R. (1998). Risk factors for prosthetic joint infection: case-control study. *Clin Infect Dis*, 27: 1247-1254.
Ref ID: 36443

29. Berrios-Torres,S.I., Yi,S.H., Bratzler,D.W., Ma,A., Mu,Y., Zhu,L. & Jernigan,J.A. (2014). Activity of commonly used antimicrobial prophylaxis regimens against pathogens causing coronary artery bypass graft and arthroplasty surgical site infections in the United States, 2006-2009. *Infect Control Hosp Epidemiol*, 35: 231-239.
Ref ID: 36267

30. Berrios-Torres,S.I., Umscheid,C.A., Bratzler,D.W., Leas,B., Stone,E.C., Kelz,R.R., Reinke,C.E., Morgan,S., Solomkin,J.S., Mazuski,J.E. & et al (2017). Centers for Disease Control and Prevention guideline for the prevention of surgical site infection, 2017. *JAMA Surg*, 152: 784-791.
Ref ID: 36174

31. Best,M.J., Buller,L.T., Gosthe,R.G., Klika,A.K. & Barsoum,W.K. (2015). Alcohol Misuse is an Independent Risk Factor for Poorer Postoperative Outcomes Following Primary Total Hip and Total Knee Arthroplasty. *J Arthroplasty*, 30: 1293-1298.
Ref ID: 37046

32. Best,M.J., Buller,L.T., Klika,A.K. & Barsoum,W.K. (2015). Outcomes following primary total hip or knee arthroplasty in substance misusers. *J Arthroplasty*, 30: 1137-1141.
Ref ID: 37048

33. Bibbo,C., Patel,D.V., Gehrmann,R.M. & Lin,S.S. (2005). Chlorhexidine provides superior skin decontamination in foot and ankle surgery: a prospective randomized study. *Clin Orthop Relat Res*, 438: 204-208.
Ref ID: 36188

34. Bierbaum,B.E., Callaghan,J.J., Galante,J.O., Rubash,H.E., Tooms,R.E. & Welch,R.B. (1999). An analysis of blood management in patients having a total hip or knee arthroplasty. *J Bone Joint Surg Am*, 81: 2-10.
Ref ID: 36857

35. Birgand,G., Saliou,P. & Lucet,J.C. (2015). Influence of staff behavior on infectious risk in operating rooms: what is the evidence? *Infect Control Hosp Epidemiol*, 36: 93-106.
Ref ID: 37004

BAIR HUGGER REFERENCE LIST
(continued)

36. Birgand,G., Toupet,G., Rukly,S., Antoniotti,G., Deschamps,M.N., Lepelletier,D., Pornet,C., Stern,J.B., Vandamme,Y.M., van der Mee-Marquet,N., Timsit,J.F. & Lucet,J.C. (2015). Air contamination for predicting wound contamination in clean surgery: A large multicenter study. *Am J Infect Control*, 43: 516-521.
Ref ID: 37002

37. Bitkover,C.Y., Marcusson,E. & Ransjo,U. (2000). Spread of coagulase-negative staphylococci during cardiac operations in a modern operating room. *Ann Thorac Surg*, 69: 1110-1115.
Ref ID: 36604

38. Bode,L.G., Kluytmans,J.A., Wertheim,H.F., Bogaers,D., Vandenbroucke-Grauls,C.M., Roosendaal,R., Troelstra,A. & et al (2010). Preventing surgical-site infections in nasal carriers of Staphylococcus aureus. *N Engl J Med*, 362: 9-17.
Ref ID: 36192

39. Bornstein,E. (2017). Eradication of staphylococcus aureus and MRSA in the Nares: A historical perspective of the ecological niche, with suggestions for future therapy considerations. *Adv Microbiol*, 7: 420-449.
Ref ID: 36990

40. Bowater,R.J., Stirling,S.A. & Lilford,R.J. (2009). Is antibiotic prophylaxis in surgery a generally effective intervention? Testing a generic hypothesis over a set of meta-analyses. *Ann Surg*, 249: 551-556.
Ref ID: 36556

41. Bozic,K.J., Lau,E., Kurtz,S., Ong,K., Rubash,H., Vail,T.P. & Berry,D.J. (2012). Patient-related risk factors for periprosthetic joint infection and postoperative mortality following total hip arthroplasty in Medicare patients. *J Bone Joint Surg Am*, 94: 794-800.
Ref ID: 36852

42. Bozic,K.J., Lau,E., Kurtz,S., Ong,K. & Berry,D.J. (2012). Patient-related risk factors for postoperative mortality and periprosthetic joint infection in medicare patients undergoing TKA. *Clin Orthop Relat Res*, 470: 130-137.
Ref ID: 36851

43. Bozic,K.J., Ong,K., Lau,E., Berry,D.J., Vail,T.P., Kurtz,S.M. & Rubash,H.E. (2013). Estimating risk in Medicare patients with THA: an electronic risk calculator for periprosthetic joint infection and mortality. *Clin Orthop Relat Res*, 471: 574-583.
Ref ID: 36880

BAIR HUGGER REFERENCE LIST

(continued)

44. Bradley,K.A., Rubinsky,A.D., Sun,H., Bryson,C.L., Bishop,M.J., Blough,D.K., Henderson,W.G. & et al (2011). Alcohol screening and risk of postoperative complications in male VA patients undergoing major non-cardiac surgery. *J Gen Intern Med*, 26: 162-169.
Ref ID: 37049

45. Brandt,C., Hott,U., Sohr,D., Daschner,F., Gastmeier,P. & Ruden,H. (2008). Operating room ventilation with laminar airflow shows no protective effect on the surgical site infection rate in orthopedic and abdominal surgery. *Ann Surg*, 248: 695-700.
Ref ID: 36215

46. Bratzler,D.W., Dellinger,E.P., Olsen,K.M., Perl,T.M., Auwaerter,P.G., Bolon,M.K., Fish,D.N., Napolitano,L.M. & et al (2013). Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health Syst Pharm*, 70: 195-283.
Ref ID: 36266

47. Brimmo,O., Glenn,M., Klika,A.K., Murray,T.G., Molloy,R.M. & Higuera,C.A. (2016). Rivaroxaban use for thrombosis prophylaxis is associated with early periprosthetic joint infection. *J Arthroplasty*, 31: 1295-1298.
Ref ID: 36348

48. Brister,A. (2011). Infection control in orthopaedic surgery. *Clin Serv J*.
Ref ID: 36262

49. Brown,M.J., Curry,T.B., Hyder,J.A., Berbari,E.F., Truty,M.J., Schroeder,D.R., Hanson,A.C. & Kor,D.J. (2017). Intraoperative Hypothermia and Surgical Site Infections in Patients with Class I/Clean Wounds: A Case-Control Study. *J Am Coll Surg*, 224: 160-171.
Ref ID: 37006

50. Buller,L.T., Rosas,S., Sabeh,K.G., Roche,M.W., McLawhorn,A.S. & Barsoum,W.K. (2018). Hypothyroidism Increases 90-Day Complications and Costs Following Primary Total Knee Arthroplasty. *J Arthroplasty*, 33: 1003-1007.
Ref ID: 36872

51. Burke,N.G., Green,C., McHugh,G., McGolderick,N., Kilcoyne,C. & Kenny,P. (2012). A prospective randomised study comparing the jubilee dressing method to a standard adhesive dressing for total hip and knee replacements. *J Tissue Viability*, 21: 84-87.
Ref ID: 36197

52. Cancienne,J.M., Patel,K.J., Browne,J.A. & Werner,B.C. (2018). Narcotic use and total knee arthroplasty. *J Arthroplasty*, 33: 113-118.
Ref ID: 36894

BAIR HUGGER REFERENCE LIST
(continued)

53. Carter,A.H., Casper,D.S., Parvizi,J. & Austin,M.S. (2012). A prospective analysis of glove perforation in primary and revision total hip and total knee arthroplasty. *J Arthroplasty*, 27: 1271-1275.
Ref ID: 37028

54. Chahal,G.S., Saithna,A., Brewster,M., Gilbody,J., Lever,S., Khan,W.S. & Foguet,P. (2013). A comparison of complications requiring return to theatre in hip and knee arthroplasty patients taking enoxaparin versus rivaroxaban for thromboprophylaxis. *Ortop Traumatol Rehabil*, 15: 125-129.
Ref ID: 36434

55. Chaiyakunapruk,N., Veenstra,D.L., Lipsky,B.A. & Saint,S. (2002). Chlorhexidine compared with povidone-iodine solution for vascular catheter-site care: a meta-analysis. *Ann Intern Med*, 136: 792-801.
Ref ID: 36186

56. Charlson,M.E., Pompei,P., Ales,K.L. & MacKenzie,C.R. (1987). A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*, 40: 373-383.
Ref ID: 37029

57. Chen,A.F., Wessel,C.B. & Rao,N. (2013). Reply to the Letter to the editor: Staphylococcus aureus screening and decolonization in orthopaedic surgery and reduction of surgical site infections. *Clin Orthop Relat Res*, 471: 3712-3713.
Ref ID: 36897

58. Chen,A.F., Wessel,C.B. & Rao,N. (2013). Staphylococcus aureus screening and decolonization in orthopaedic surgery and reduction of surgical site infections. *Clin Orthop Relat Res*, 471: 2383-2399.
Ref ID: 36204

59. Chen,J., Cui,Y., Li,X., Miao,X., Wen,Z., Xue,Y. & Tian,J. (2013). Risk factors for deep infection after total knee arthroplasty: a meta-analysis. *Arch Orthop Trauma Surg*, 133: 675-687.
Ref ID: 37030

60. Cherifi,S., Byle,B., Deplano,A., Nonhoff,C., Denis,O. & Hallin,M. (2013). Comparative epidemiology of Staphylococcus epidermidis isolates from patients with catheter-related bacteremia and from healthy volunteers. *J Clin Microbiol*, 51: 1541-1547.
Ref ID: 36603

BAIR HUGGER REFERENCE LIST

(continued)

61. Chrastil,J., Anderson,M.B., Stevens,V., Anand,R., Peters,C.L. & Pelt,C.E. (2015). Is Hemoglobin A1c or Perioperative Hyperglycemia Predictive of Periprosthetic Joint Infection or Death Following Primary Total Joint Arthroplasty? *J Arthroplasty*, 30: 1197-1202.
Ref ID: 36953

62. Clarke,J.V., Deakin,A.H., Dillon,J.M., Emmerson,S. & Kinninmonth,A.W. (2009). A prospective clinical audit of a new dressing design for lower limb arthroplasty wounds. *J Wound Care*, 18: 5-8.
Ref ID: 36196

63. Cloke,D.J. & Partington,P.F. (2007). Wound complications in elective orthopaedics: are current British national data relevant? *Ann R Coll Surg Engl*, 89: 41-43.
Ref ID: 36445

64. Coello,R., Charlett,A., Wilson,J., Ward,V., Pearson,A. & Borriello,P. (2005). Adverse impact of surgical site infections in English hospitals. *J Hosp Infect*, 60: 93-103.
Ref ID: 36875

65. Cole,P. (1997). Casualty in epidemiology, health policy, and law. *Environ Law Rep*, 27: 10279-10285.
Ref ID: 36224

66. Conlon,N.P., Bale,E.P., Herbison,G.P. & McCarroll,M. (2008). Postoperative anemia and quality of life after primary hip arthroplasty in patients over 65 years old. *Anesth Analg*, 106: 1056-1061.
Ref ID: 36858

67. Cordero-Ampuero,J. & de Dios,M. (2010). What are the risk factors for infection in hemiarthroplasties and total hip arthroplasties? *Clin Orthop Relat Res*, 468: 3268-3277.
Ref ID: 36447

68. Courville,X.F., Tomek,I.M., Kirkland,K.B., Birhle,M., Kantor,S.R. & Finlayson,S.R. (2012). Cost-effectiveness of preoperative nasal mupirocin treatment in preventing surgical site infection in patients undergoing total hip and knee arthroplasty: a cost-effectiveness analysis. *Infect Control Hosp Epidemiol*, 33: 152-159.
Ref ID: 36221

69. Cox,D.R. (2005). Some challenges for medical statistics. *Eur J Epidemiol*, 20: 5-9.
Ref ID: 36222

BAIR HUGGER REFERENCE LIST
(continued)

70. Cozowicz,C., Olson,A., Poeran,J., Morwald,E.E., Zubizarreta,N., Girardi,F.P., Hughes,A.P. & et al (2017). Opioid prescription levels and postoperative outcomes in orthopedic surgery. *Pain*, 158: 2422-2430.
Ref ID: 36905

71. Daines,B.K., Dennis,D.A. & Amann,S. (2015). Infection prevention in total knee arthroplasty. *J Am Acad Orthop Surg*, 23: 356-364.
Ref ID: 36910

72. Darouiche,R.O., Wall,M.J., Jr., Itani,K.M., Otterson,M.F., Webb,A.L., Carrick,M.M., Miller,H.J. & etal (2010). Chlorhexidine-alcohol versus povidone-iodine for surgical-site antisepsis. *N Engl J Med*, 362: 18-26.
Ref ID: 36193

73. Darouiche,R.O., Green,D.M., Harrington,M.A., Ehni,B.L., Kougias,P., Bechara,C.F. & O'Connor,D.P. (2017). Association of Airborne Microorganisms in the Operating Room With Implant Infections: A Randomized Controlled Trial. *Infect Control Hosp Epidemiol*, 38: 3-10.
Ref ID: 36200

74. De Vito,P., Incerpi,S., Pedersen,J.Z., Luly,P., Davis,F.B. & Davis,P.J. (2011). Thyroid hormones as modulators of immune activities at the cellular level. *Thyroid*, 21: 879-890.
Ref ID: 36854

75. De Vito,P., Balducci,V., Leone,S., Percario,Z., Mangino,G., Davis,P.J., Davis,F.B., Affabris,E., Luly,P., Pedersen,J.Z. & Incerpi,S. (2012). Nongenomic effects of thyroid hormones on the immune system cells: New targets, old players. *Steroids*, 77: 988-995.
Ref ID: 36853

76. Del Bono,R., Martini,G. & Volpi,R. (2011). Update on low molecular weight heparins at the beginning of third millennium. Focus on reviparin. *Eur Rev Med Pharmacol Sci*, 15: 950-959.
Ref ID: 36730

77. Dellinger,E.P., Hausmann,S.M., Bratzler,D.W., Johnson,R.M., Daniel,D.M., Bunt,K.M., Baumgardner,G.A. & Sugarman,J.R. (2005). Hospitals collaborate to decrease surgical site infections. *Am J Surg*, 190: 9-15.
Ref ID: 36551

78. Deyo,R.A., Cherkin,D.C. & Ciol,M.A. (1992). Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol*, 45: 613-619.
Ref ID: 36976

BAIR HUGGER REFERENCE LIST

(continued)

79. Dguzeh,U., Haddad,N.C., Smith,K.T.S., Johnson,J.O., Doye,A.A., Gwathmey,J.K. & Haddad,G.E. (2018). Alcoholism: A multi-systemic cellular insult to organs. *Int J Environ Res Public Health*, 15.
Ref ID: 37050

80. Diab-Elschahawi,M., Berger,J., Blacky,A., Kimberger,O., Oguz,R., Kuelpmann,R., Kramer,A. & Assadian,O. (2011). Impact of different-sized laminar air flow versus no laminar air flow on bacterial counts in the operating room during orthopedic surgery. *Am J Infect Control*, 39: e25-e29.
Ref ID: 36334

81. Dodds Ashley,E.S., Carroll,D.N., Engemann,J.J., Harris,A.D., Fowler,V.G., Jr., Sexton,D.J. & Kaye,K.S. (2004). Risk factors for postoperative mediastinitis due to methicillin-resistant Staphylococcus aureus. *Clin Infect Dis*, 38: 1555-1560.
Ref ID: 36528

82. Dowsey,M.M. & Choong,P.F. (2008). Obesity is a major risk factor for prosthetic infection after primary hip arthroplasty. *Clin Orthop Relat Res*, 466: 153-158.
Ref ID: 36538

83. Dowsey,M.M., Liew,D., Stoney,J.D. & Choong,P.F.M. (2010). The impact of obesity on weight change and outcomes at 12 months in patients undergoing total hip arthroplasty. *Med J Aust*, 193: 17-21.
Ref ID: 37025

84. Dwyer-Lindgren,L., Mackenbach,J.P., van Lenthe,F.J., Flaxman,A.D. & Mokdad,A.H. (2016). Diagnosed and undiagnosed diabetes prevalence by county in the U.S., 1999-2012. *Diabetes Care*, 39: 1556-1562.
Ref ID: 36956

85. Eckmanns,T., Bessert,J., Behnke,M., Gastmeier,P. & Ruden,H. (2006). Compliance with antiseptic hand rub use in intensive care units: the Hawthorne effect. *Infect Control Hosp Epidemiol*, 27: 931-934.
Ref ID: 36260

86. ECRI Institute (2013). Forced-air warming and surgical site infections. *Medical Devices*, (April): 122-125.
Ref ID: 36214

87. Edmiston,C.E., Krepel,C., Kelly,H., Larson,J., Andris,D., Hennen,C., Nakeeb,A. & Wallace,A.F. (2004). Perioperative antibiotic prophylaxis in the gastric bypass patient: do we achieve therapeutic levels? *Surgery*, 136: 738-747.
Ref ID: 36535

BAIR HUGGER REFERENCE LIST
(continued)

88. Egger,M., Schneider,M. & Davey Smith,G. (1998). Spurious precision? Meta-analysis of observational studies. *BMJ*, 316: 140-144.
Ref ID: 36240

89. Elixhauser,A., Steiner,C., Harris,D.R. & Coffey,R.M. (1998). Comorbidity measures for use with administrative data. *Medical Care*, 36: 8-27.
Ref ID: 36963

90. England,S.P., Stern,S.H., Insall,J.N. & Windsor,R.E. (1990). Total knee arthroplasty in diabetes mellitus. *Clin Orthop Relat Res*, 260: 130-134.
Ref ID: 36466

91. Eriksson,B.I., Borris,L.C., Friedman,R.J., Haas,S., Huisman,M.V., Kakkar,A.K., Bandel,T.J. & et al (2008). Rivaroxaban versus enoxaparin for thromboprophylaxis after hip arthroplasty. *N Engl J Med*, 358: 2765-2775.
Ref ID: 36175

92. Falagas,M.E. & Kompoti,M. (2006). Obesity and infection. *Lancet Infect Dis*, 6: 438-446.
Ref ID: 36518

93. Falagas,M.E. & Karageorgopoulos,D.E. (2010). Adjustment of dosing of antimicrobial agents for bodyweight in adults. *Lancet*, 375: 248-251.
Ref ID: 36536

94. Fender,D., Harper,W.M. & Gregg,P.J. (1999). Outcome of Charnley total hip replacement across a single health region in England: the results at five years from a regional hip register. *J Bone Joint Surg Br*, 81: 577-581.
Ref ID: 36172

95. Forey,B.A., Thornton,A.J. & Lee,P.N. (2011). Systematic review with meta-analysis of the epidemiological evidence relating smoking to COPD, chronic bronchitis and emphysema. *BMC Pulm Med*, 11: 36-97.
Ref ID: 36565

96. Forse,R.A., Karam,B., MacLean,L.D. & Christou,N.V. (1989). Antibiotic prophylaxis for surgery in morbidly obese patients. *Surgery*, 106: 750-756.
Ref ID: 36558

97. Frank,S.M., Fleisher,L.A., Breslow,M.J., Higgins,M.S., Olson,K.F., Kelly,S. & Beattie,C. (1997). Perioperative maintenance of normothermia reduces the incidence of morbid cardiac events. A randomized clinical trial. *J Am Med Assoc*, 277: 1127-1134.
Ref ID: 37007

BAIR HUGGER REFERENCE LIST
(continued)

98. Frisch,N.B., Pepper,A.M., Rooney,E. & Silverton,C. (2017). Intraoperative hypothermia in total hip and knee arthroplasty. *Orthopedics*, 40: 56-63.
Ref ID: 36273

99. Gade,N.S. & Qazi,M.S. (2014). Recent trends of aminoglycoside resistance among Staphylococcus aureus isolates in tertiary care hospital. *J Microbiol Antimicrobiol*, 6: 96.
Ref ID: 36258

100. Galanakos,S.P., Monteiro,F.J. & Ferraz,M.P. (2009). Biofilm and orthopaedic practice; the world of microbes in a world of implants. *J Ortho Trauma*, 23: 175-179.
Ref ID: 36347

101. Galat,D.D., McGovern,S.C., Larson,D.R., Harrington,J.R., Hanssen,A.D. & Clark,H.D. (2009). Surgical treatment of early wound complications following primary total knee arthroplasty. *J Bone Joint Surg Am*, 91: 48-54.
Ref ID: 36915

102. Gehrke,T. & Parvizi,J. (2014). Proceedings of the international consensus meeting on periprosthetic joint infection. *J Arthroplasty*, 29: 4.
Ref ID: 36731

103. George,P.M. (1996). Case against antibiotic prophylaxis for endocarditis and prosthesis infection in dermatologic procedures involving uninfected skin. *J Am Acad Dermatol*, 34: 153-154.
Ref ID: 36668

104. Gillson,J. & Lowdon,G. (2014). Implementing effective SSI surveillance. *Clin Serv J*, 71-74.
Ref ID: 36166

105. Glass,T.A., Goodman,S.N., Hernan,M.A. & Samet,J.M. (2013). Causal inference in public health. *Annu Rev Public Health*, 34: 61-75.
Ref ID: 34920

106. Glenny,A.M. & Song,F. (1999). Antimicrobial prophylaxis in total hip replacement: a systematic review. *Health Technol Assess*, 3: 1-57.
Ref ID: 36595

107. Goodman,S.M., Springer,B., Guyatt,G. & et al. (2017). 2017 American College of Rheumatology/American Association of Hip and Knee Surgeons Guideline for the Perioperative Management of Antirheumatic Medication in Patients With Rheumatic Diseases Undergoing Elective Total Hip or Total Knee Arthroplasty. *J Arthroplasty*, 32: 2628-2638.
Ref ID: 36918

BAIR HUGGER REFERENCE LIST
(continued)

108. Goodnough,L.T., Vizmeg,K., Sobecks,R., Schwarz,A. & Soegiarso,W. (1992). Prevalence and classification of anemia in elective orthopedic surgery patients: implications for blood conservation programs. *Vox Sang*, 63: 90-95.
Ref ID: 36860

109. Goodnough,L.T., Maniatis,A., Earnshaw,P., Benoni,G., Beris,P., Bisbe,E., Fergusson,D.A. & et al (2011). Detection, evaluation, and management of preoperative anaemia in the elective orthopaedic surgical patient: NATA guidelines. *Br J Anaesth*, 106: 13-22.
Ref ID: 36859

110. Gordon,S.M., Culver,D.H., Simmons,B.P. & Jarvis,W.R. (1990). Risk factors for wound infections after total knee arthroplasty. *Am J Epidemiol*, 131: 905-916.
Ref ID: 36351

111. Graves,N., Wloch,C., Wilson,J., Barnett,A., Sutton,A., Cooper,N., Merollini,K., McCreanor,V., Cheng,Q. & et al (2016). A cost-effectiveness modelling study of strategies to reduce risk of infection following primary hip replacement based on a systematic review. *Health Technol Assess*, 20: 1-144.
Ref ID: 36219

112. Greene,K.A., Wilde,A.H. & Stulberg,B.N. (1991). Preoperative nutritional status of total joint patients. Relationship to postoperative wound complications. *J Arthroplasty*, 6: 321-325.
Ref ID: 36207

113. Greenky,M., Gandhi,K., Pulido,L., Restrepo,C. & Parvizi,J. (2012). Preoperative anemia in total joint arthroplasty: is it associated with periprosthetic joint infection? *Clin Orthop Relat Res*, 470: 2695-2701.
Ref ID: 36846

114. Greenland,S. & Robins,J.M. (1986). Identifiability, exchangeability, and epidemiological confounding. *Int J Epidemiol*, 15: 413-419.
Ref ID: 37024

115. Greenland,S. & Robins,J.M. (2000). Epidemiologoy, Justice and the Probability of Causation. *Jurimetrics*, 40: 321-340.
Ref ID: 36337

116. Greenland,S. & Robins,J.M. (2009). Identifiability, exchangeability and confounding revisited. *Epidemiol Perspect Innov*, 6: 4.
Ref ID: 36339

BAIR HUGGER REFERENCE LIST
(continued)

117. Grunfeld,R., Kunselman,A., Bustillo,J. & Juliano,P.J. (2011). Wound complications in thyroxine-supplemented patients following foot and ankle surgery. *Foot Ankle Int*, 32: 38-46.
Ref ID: 36856

118. Haas,A.F. & Grekin,R.C. (1995). Antibiotic prophylaxis in dermatologic surgery. *J Am Acad Dermatol*, 32: 155-176.
Ref ID: 36661

119. Hacek,D.M., Robb,W.J., Paule,S.M., Kudrna,J.C., Stamos,V.P. & Peterson,L.R. (2008). Staphylococcus aureus nasal decolonization in joint replacement surgery reduces infection. *Clin Orthop Relat Res*, 466: 1349-1355.
Ref ID: 36580

120. Haeberle,H.S., Navarro,S.M., Samuel,L.T., Khlopas,A., Sultan,A.A., Sodhi,N., Chughtai,M., Mont,M.A. & Ramkumar,P.N. (2017). No Evidence of Increased Infection Risk with Forced-Air Warming Devices: A Systematic Review. *Surg Technol Int*, 31: 295-301.
Ref ID: 36599

121. Halm,E.A., Wang,J.J., Boockvar,K., Penrod,J., Silberzweig,S.B., Magaziner,J., Koval,K.J. & Siu,A.L. (2004). The effect of perioperative anemia on clinical and functional outcomes in patients with hip fracture. *J Orthop Trauma*, 18: 369-374.
Ref ID: 36861

122. Halpern,A.C., Leyden,J.J., Dzubow,L.M. & McGinley,K.J. (1988). The incidence of bacteremia in skin surgery of the head and neck. *J Am Acad Dermatol*, 19: 112-116.
Ref ID: 36658

123. Harle,S., Korhonen,A., Kettunen,J.A. & Seitsalo,S. (2005). A randomised clinical trial of two different wound dressing materials for hip replacement patients. *J Orthop Nurs*, 9: 205-210.
Ref ID: 36198

124. Harris,A.H., Reeder,R., Ellerbe,L., Bradley,K.A., Rubinsky,A.D. & Giori,N.J. (2011). Preoperative alcohol screening scores: association with complications in men undergoing total joint arthroplasty. *J Bone Joint Surg Am*, 93: 321-327.
Ref ID: 37051

125. Harris,A.H., Bowe,T.R., Gupta,S., Ellerbe,L.S. & Giori,N.J. (2013). Hemoglobin A1C as a marker for surgical risk in diabetic patients undergoing total joint arthroplasty. *J Arthroplasty*, 28 (Suppl 8): 25-29.
Ref ID: 36945

BAIR HUGGER REFERENCE LIST
(continued)

126. Haverkamp,D., Klinkenbijl,M.N., Somford,M.P., Albers,G.H. & van der Vis,H.M. (2011). Obesity in total hip arthroplasty--does it really matter? A meta-analysis. *Acta Orthop*, 82: 417-422.
Ref ID: 36474

127. He,X., Karra,S., Pakseresht,P., Apte,S.V. & Elgobashi,S. (2018). Effect of heated-air blanket on the dispersion of squames in an operating room. *Int J Numer Meth Biomed Engeng*, 34 : e2960.
Ref ID: 37000

128. Heal,C., Buettner,P. & Browning,S. (2006). Risk factors for wound infection after minor surgery in general practice. *Med J Aust*, 185: 255-258.
Ref ID: 36670

129. Healy,L.A., Ryan,A.M., Sutton,E., Younger,K., Mehigan,B., Stephens,R. & Reynolds,J.V. (2010). Impact of obesity on surgical and oncological outcomes in the management of colorectal cancer. *Int J Colorectal Dis*, 25: 1293-1299.
Ref ID: 36527

130. Hebert,C. & Robicsek,A. (2010). Decolonization therapy in infection control. *Curr Opin Infect Dis*, 23: 340-345.
Ref ID: 36578

131. Hellmark,B., Soderquist,B., Unemo,M. & Nilsdotter-Augustinsson,A. (2013). Comparison of Staphylococcus epidermidis isolated from prosthetic joint infections and commensal isolates in regard to antibiotic susceptibility, agr type, biofilm production, and epidemiology. *Int J Med Microbiol*, 303: 32-39.
Ref ID: 36601

132. Hereford,T.E., Cryar,K.A., Edwards,P.K., Siegel,E.R., Barnes,C.L. & Mears,S.C. (2018). Patients with hip or knee arthritis underreport narcotic usage. *J Arthroplasty*, still in print.
Ref ID: 36972

133. Hervey,S.L., Purves,H.R., Guller,U., Toth,A.P., Vail,T.P. & Pietrobon,R. (2003). Provider volume of total knee arthroplasties and patient outcomes in the HCUP-Nationwide Inpatient Sample. *J Bone Joint Surg Am*, 85-A: 1775-1783.
Ref ID: 36898

134. Herwalt,L.A., Cullen,J.J., French,P., Hu,J., Pfaller,M.A., Wenzel,R.P. & Perl,T.M. (2004). Preoperative risk factors for nasal carriage of Staphylococcus aureus. *Infect Control Hosp Epidemiol*, 25: 481-484.
Ref ID: 36529

BAIR HUGGER REFERENCE LIST
(continued)

135. Hickson,C.J., Metcalfe,D., Elgohari,S., Owald,T., Masters,J.P., Rymaszewska,M., Reed,M.R. & Sprowson,A.P. (2015). Prophylactic antibiotics in elective hip and knee arthroplasty: an analysis of organisms reported to cause infections and National survey of clinical practice. *Bone Joint Res*, 4: 181-189.
Ref ID: 36201

136. Hollowell,J.G., Staehling,N.W., Flanders,W.D., Hannon,W.H., Gunter,E.W., Spencer,C.A. & Braverman,L.E. (2002). Serum TSH,T_4, and thyroid antibodies in the United States Population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). *J Clin Endocrinol Metab*, 87: 489-499.
Ref ID: 20181

137. Hooper,G.J., Rothwell,A.G., Frampton,C. & Wyatt,M.C. (2011). Does the use of laminar flow and space suits reduce early deep infection after total hip and knee replacement?: the ten-year results of the New Zealand Joint Registry. *J Bone Joint Surg Br*, 93: 85-90.
Ref ID: 36170

138. Huotari,K., Agthe,N. & Lyytikainen,O. (2007). Validation of surgical site infection surveillance in orthopedic procedures. *Am J Infect Control*, 35: 216-221.
Ref ID: 36948

139. Huttunen,R., Laine,J., Lumio,J., Vuento,R. & Syrjanen,J. (2007). Obesity and smoking are factors associated with poor prognosis in patients with bacteraemia. *BMC Infect Dis*, 7: 13.
Ref ID: 36685

140. Huttunen,R. & Syrjanen,J. (2013). Obesity and the risk and outcome of infection. *Int J Obes (Lond)*, 37: 333-340.
Ref ID: 36522

141. Huttunen,R., Karppelin,M. & Syrjanen,J. (2013). Obesity and nosocomial infections. *J Hosp Infect*, 85: 8-16.
Ref ID: 36521

142. Iorio,R., Williams,K.M. & Marcantonio,A.J. (2018). Diabetes mellitus, hemoglobin A1C, and the incidence of total joint arthroplasty infection. *J Arthroplasty*, 27: 726-729.
Ref ID: 36951

143. Jakobsen,T.H., Eickhardt,S.R., Gheorghe,A.G., Stenqvist,C., Sonderholm,M., Stavnsberg,C., Jensen,P.O. & et al (2018). Implants induce a new niche for microbiomes. *APMIS*, still in print.
Ref ID: 36826

BAIR HUGGER REFERENCE LIST
(continued)

144. Jameson,S.S., Rymaszewska,M., Hui,A.C., James,P., Serrano-Pedraza,I. & Muller,S.D. (2012). Wound complications following rivaroxaban administration: a multicenter comparison with low-molecular-weight heparins for thromboprophylaxis in lower limb arthroplasty. *J Bone Joint Surg Am*, 94: 1554-1558.
Ref ID: 36163

145. Jameson,S.S., Baker,P.N., Deehan,D.J., Port,A. & Reed,M.R. (2014). Evidence-base for aspirin as venous thromboembolic prophylaxis following joint replacement. *Bone Joint Res*, 3: 146-149.
Ref ID: 36165

146. Jameson,S.S. & Reed,M.R. (2016). Prevention of Periprosthetic Joint Infection: What is the Current Envidence? In: Kendoff,D., Morgan-Jones,R. & Haddad,F.S. (Eds.), *Periprosthetic Joint Infections. Changing Paradigms*, pp. 45-59. Swizerland: Springer. 59 pp.
Ref ID: 36965

147. Jamsen,E., Nevalainen,P., Eskelinen,A., Huotari,K., Kalliovalkama,J. & Moilanen,T. (2012). Obesity, diabetes, and preoperative hyperglycemia as predictors of periprosthetic joint infection: a single-center analysis of 7181 primary hip and knee replacements for osteoarthritis. *J Bone Joint Surg Am*, 94: e101-1-e101-9.
Ref ID: 36933

148. Janson,B. & Thursky,K. (2012). Dosing of antibiotics in obesity. *Curr Opin Infect Dis*, 25: 634-649.
Ref ID: 36591

149. Jeans,E., Holleyman,R., Tate,D., Reed,M. & Malviya,A. (2018). Methicillin sensitive staphylococcus aureus screening and decolonisation in elective hip and knee arthroplasty. *J Infect*, still in print.
Ref ID: 36873

150. Jensen,C.D., Steval,A., Partington,P.F., Reed,M.R. & Muller,S.D. (2011). Return to theatre following total hip and knee replacement, before and after the introduction of rivaroxaban: a retrospective cohort study. *J Bone Joint Surg Br*, 93: 91-95.
Ref ID: 36164

151. Jiang,J., Teng,Y., Fan,Z., Khan,S. & Xia,Y. (2014). Does obesity affect the surgical outcome and complication rates of spinal surgery? A meta-analysis. *Clin Orthop Relat Res*, 472: 968-975.
Ref ID: 36519

152. Johnson,A.J., Kapadia,B.H., Daley,J.A., Molina,C.B. & Mont,M.A. (2013). Chlorhexidine reduces infections in kneee arthroplasty. *J Knee Surg*, 26: 213-218.
Ref ID: 36912

BAIR HUGGER REFERENCE LIST
(continued)

153. Johnson,R., Jameson,S.S., Sanders,R.D., Sargant,N.J., Muller,S.D., Meek,R.M. & Reed,M.R. (2013). Reducing surgical site infection in arthroplasty of the lower limb: A multi-disciplinary approach. *Bone Joint Res*, 2: 58-65.
Ref ID: 36208

154. Jonklaas,J., Bianco,A.C., Bauer,A.J., Burman,K.D., Cappola,A.R., Celi,F.S., Cooper,D.S. & etal (2014). Guidelines for the treatment of hypothyroidism: prepared by the american thyroid association task force on thyroid hormone replacement. *Thyroid*, 24: 1670-1751.
Ref ID: 37039

155. Jonsson,E.O., Johannesdottir,H., Robertsson,O. & Mogensen,B. (2014). Bacterial contamination of the wound during primary total hip and knee replacement. Median 13 years of follow-up of 90 replacements. *Acta Orthop*, 85: 159-164.
Ref ID: 36602

156. Jonsson,K., Jensen,J.A., Goodson,W.H. & et al. (1991). Tissue oxygenation, anemia, and perfusion in relation to wound healing in surgical patients. *Ann Surg*, 214: 605-613.
Ref ID: 36917

157. Just,B., Trevien,V., Delva,E. & Lienhart,A. (1993). Prevention of intraoperative hypothermia by preoperative skin-surface warming. *Anesthesiology*, 79: 214-218.
Ref ID: 36435

158. Kabon,B., Nagele,A., Reddy,D., Eagon,C., Fleshman,J.W., Sessler,D.I. & Kurz,A. (2004). Obesity decreases perioperative tissue oxygenation. *Anesthesiology*, 100: 274-280.
Ref ID: 36555

159. Kakkar,A.K., Brenner,B., Dahl,O.E., Eriksson,B.I., Mouret,P., Muntz,J., Soglian,A.G. & et al (2008). Extended duration rivaroxaban versus short-term enoxaparin for the prevention of venous thromboembolism after total hip arthroplasty: a double-blind, randomised controlled trial. *Lancet*, 372: 31-39.
Ref ID: 36177

160. Kalmeijer,M.D., van Nieuwland-Bollen,E., Bogaers-Hofman,D. & de Baere,G.A. (2000). Nasal carriage of staphylococcus aureus is a major risk factor for surgical-site infections in orthopedic surgery. *Infect Control Hosp Epidemiol*, 21: 319-323.
Ref ID: 36902

161. Kalmeijer,M.D., Coertjens,H., van Nieuwland-Bollen,P.M. & et al (2002). Surgical site infections in orthopedic surgery: the effect of mupirocin nasal ointment in a double-blind, randomized, placebo-controlled study. *Clin Infect Dis*, 35: 353-358.
Ref ID: 36899

BAIR HUGGER REFERENCE LIST
(continued)

162. Karpanen,T.J., Worthington,T., Conway,B.R., Hilton,A.C., Elliott,T.S.J. & Lambert,P.A. (2008). Penetration of chlorhexidine into human skin. *Antimicrob Agents Chemother*, 52: 3633-3636.
Ref ID: 36992

163. Kaye,K.S., Marchaim,D., Chen,T.Y., Chopra,T., Anderson,D.J., Choi,Y., Sloane,R. & Schmader,K.E. (2011). Predictors of nosocomial bloodstream infections in older adults. *J Am Geriatr Soc*, 59: 622-627.
Ref ID: 36533

164. Kellam,M.D., Dieckmann,L.S. & Austin,P.N. (2013). Forced-air warming devices and the risk of surgical site infections. *AORN J*, 98: 353-366.
Ref ID: 36279

165. Kendoff,D., Morgan-Jones,R. & Haddad,F.S. (2018). *Periprosthetic Joint Infections. Changing Paradigms*. Switzerland: Springer.
Ref ID: 36964

166. Kerkhoffs,G.M., Servien,E., Dunn,W., Dahm,D., Bramer,J.A. & Haverkamp,D. (2012). The influence of obesity on the complication rate and outcome of total knee arthroplasty: a meta-analysis and systematic literature review. *J Bone Joint Surg Am*, 94: 1839-1844.
Ref ID: 36516

167. Khan,S.K., Malviya,A., Muller,S.D., Carluke,I., Partington,P.F., Emmerson,K.P. & Reed,M.R. (2014). Reduced short-term complications and mortality following Enhanced Recovery primary hip and knee arthroplasty: results from 6,000 consecutive procedures. *Acta Orthop*, 85: 26-31.
Ref ID: 36436

168. Kim,D.H., Spencer,M., Davidson,S.M., Li,L., Shaw,J.D., Gulczynski,D., Hunter,D.J. & et al (2010). Institutional prescreening for detection and eradication of methicillin-resistant Staphylococcus aureus in patients undergoing elective orthopaedic surgery. *J Bone Joint Surg Am*, 92: 1820-1826.
Ref ID: 36876

169. Kim,J.H., Lim,K.M. & Gwak,H.S. (2017). New anticoagulants for the prevention and treatment of venous thromboembolism. *Biomol Ther*, 25: 461-470.
Ref ID: 36729

170. Kong,L., Cao,J., Zhang,Y., Ding,W. & Shen,Y. (2017). Risk factors for periprosthetic joint infection following primary total hip or knee arthroplasty: a meta-analysis. *Int Wound J*, 14: 529-536.
Ref ID: 37053

BAIR HUGGER REFERENCE LIST
(continued)

171. Kunutsor,S.K., Whitehouse,M.R., Blom,A.W. & Beswick,A.D. (2016). Patient-related risk factors for periprosthetic joint infection after total joint arthroplasty: A systematic review and meta-analysis. *PloS One*, 11: e0150866.
Ref ID: 36483

172. Kurz,A., Sessler,D.I. & Lenhardt,R. (1996). Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. *N Engl J Med*, 334: 1209-1215.
Ref ID: 36274

173. Kurz,A. (2008). Thermal care in the perioperative period. *Best Pract Res Clin Anaesthesiol*, 22: 39-62.
Ref ID: 36594

174. Lagiou,P., Adami,H.O. & Trichopoulos,D. (2005). Causality in cancer epidemiology. *Eur J Epidemiol*, 20: 565-574.
Ref ID: 36184

175. Lai,K., Bohm,E.R., Burnell,C. & Hedden,D.R. (2007). Presence of medical comorbidities in patients with infected primary hip or knee arthroplasties. *J Arthroplasty*, 22: 651-656.
Ref ID: 36476

176. Lamagni,T., Elgohari,S. & Harrington,P. (2015). Trends in surgical site infections following orthopaedic surgery. *Curr Opin Infect Dis*, 28: 125-132.
Ref ID: 36205

177. Lange-Asschenfeldt,B., Marenbach,D., Lang,C., Patzelt,A., Ulrich,M. & et al (2011). Distribution of bacteria in the epidermal layers and hair follicles of the human skin. *Skin Pharmacol Physiol*, 24: 305-311.
Ref ID: 36993

178. Lassen,M.R., Ageno,W., Borris,L.C., Lieberman,J.R., Rosencher,N., Bandel,T.J., Misselwitz,F. & et al (2008). Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty. *N Engl J Med*, 358: 2776-2786.
Ref ID: 36178

179. Lebowitz,M.D. (1981). Respiratory symptoms and disease related to alcohol consumption. *Am Rev Respir Dis*, 123: 16-19.
Ref ID: 37018

180. Legg,A.J., Cannon,T. & Hamer,A.J. (2012). Do forced air patient-warming devices disrupt unidirectional downward airflow? *J Bone Joint Surg Br*, 94: 254-256.
Ref ID: 37001

BAIR HUGGER REFERENCE LIST

(continued)

181. Leijtens,B., Koeter,M., Kremers,K. & Koeter,S. (2013). High incidence of postoperative hypothermia in total knee and total hip arthroplasty: a prospective observational study. *J Arthroplasty*, 28: 895-898.
Ref ID: 36607

182. Lenguerrand,E., Whitehouse,M.R., Beswick,A.D., Kunutsor,S.K., Burston,B., Porter,M. & Blom,A.W. (2018). Risk factors associated with revision for prosthetic joint infection after hip replacement: a prospective observational cohort study. *Lancet Infect Dis*, still in print.
Ref ID: 36969

183. Lenguerrand,E., Beswick,A.D., Whitehouse,M.R., Wylde,V. & Blom,A.W. (2018). Outcomes following hip and knee replacement in diabetic versus nondiabetic patients and well versus poorly controlled diabetic patients: a prospective cohort study. *Acta Orthop*, 89: 399-405.
Ref ID: 36971

184. Li,X., Li,M., Li,J., Gong,W., Sun,Y., Tang,J., Yao,X. & Wang,X. (2017). Glove perforation and contamination in fracture fixation surgeries. *Am J Infect Control*, 45: 458-460.
Ref ID: 36989

185. Lindsey Lupo,B. (2018). Comparing Forced-Air to Resistive-Polymer Warming for Perioperative Temperature Management: A Retrospective Study. pp. 1-46. Western Carolina University (WCU). 46 pp.
Ref ID: 37031

186. Liu,W., Wahafu,T., Cheng,M., Cheng,T., Zhang,Y. & Zhang,X. (2015). The influence of obesity on primary total hip arthroplasty outcomes: A meta-analysis of prospective cohort studies. *Orthop Traumatol Surg Res*, 101: 289-296.
Ref ID: 36473

187. Lowy,F.D. (1998). Staphylococcus aureus infections. *N Engl J Med*, 339: 520-532.
Ref ID: 36254

188. Lubbeke,A., Stern,R., Garavaglia,G., Zurcher,L. & Hoffmeyer,P. (2007). Differences in outcomes of obese women and men undergoing primary total hip arthroplasty. *Arthritis Rheum*, 57: 327-334.
Ref ID: 36472

189. Lubbeke,A., Moons,K.G., Garavaglia,G. & Hoffmeyer,P. (2008). Outcomes of obese and nonobese patients undergoing revision total hip arthroplasty. *Arthritis Rheum*, 59: 738-745.
Ref ID: 36471

BAIR HUGGER REFERENCE LIST
(continued)

190. Ma,X.X., Wang,E.H., Liu,Y. & Luo,E.J. (2011). Antibiotic susceptibility of coagulase-negative staphylococci (CoNS): emergence of teicoplanin-non-susceptible CoNS strains with inducible resistance to vancomycin. *J Med Microbiol*, 60: 1661-1668.
Ref ID: 36265

191. Maclure,M. & Schneeweiss,S. (2001). Causation of bias: the episcope. *Epidemiology*, 12: 114-122.
Ref ID: 37019

192. Malani,P.N. (2015). Bundled approaches for surgical site infection prevention: the continuing quest to get to zero. *J Am Med Assoc*, 313: 2131-2132.
Ref ID: 36597

193. Maldonado,G. (2016). The role of counterfactual theory in casual reasoning. *Ann Epidemiol*, 26: 681-682.
Ref ID: 36340

194. Mangram,A.J., Horan,T.C., Pearson,M.L., Silver,L.C. & Jarvis,W.R. (1999). Guideline for Prevention of Surgical Site Infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. *Am J Infect Control*, 27: 97-132.
Ref ID: 36168

195. Mangram,A.J., Horan,T.C., Pearson,M.L., Silver,L.C. & Jarvis,W.R. (1999). Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol*, 20: 250-278.
Ref ID: 28713

196. Mansson,E., Hellmark,B., Sundqvist,M. & Soderquist,B. (2015). Sequence types of Staphylococcus epidermidis associated with prosthetic joint infections are not present in the laminar airflow during prosthetic joint surgery. *APMIS*, 123: 589-595.
Ref ID: 36600

197. Mantilla,C.B., Wass,C.T., Goodrich,K.A., Johanns,C.J., Kool,M.L., Zhu,X., Corredor,J.A., Warner,D.O., Joyner,M.J. & et al (2011). Risk for perioperative myocardial infarction and mortality in patients undergoing hip or knee arthroplasty: the role of anemia. *Transfusion*, 51: 82-91.
Ref ID: 36862

198. Maradit Kremers,H., Lewallen,L.W., Mabry,T.M., Berry,D.J., Berbari,E.F. & Osmon,D.R. (2015). Diabetes mellitus, hyperglycemia, hemoglobin A1C and the risk of prosthetic joint infections in total hip and knee arthroplasty. *J Arthroplasty*, 30: 439-443.
Ref ID: 36952

BAIR HUGGER REFERENCE LIST
(continued)

199. Maragh,S.L., Otley,C.C., Roenigk,R.K. & Phillips,P.K. (2005). Antibiotic prophylaxis in dermatologic surgery: updated guidelines. *Dermatol Surg*, 31: 83-91.
Ref ID: 36663

200. Marchant,M.H., Jr., Viens,N.A., Cook,C., Vail,T.P. & Bolognesi,M.P. (2009). The impact of glycemic control and diabetes mellitus on perioperative outcomes after total joint arthroplasty. *J Bone Joint Surg Am*, 91: 1621-1629.
Ref ID: 36949

201. McAninch,E.A., Rajan,K.B., Miller,C.H. & Bianco,A.C. (2018). Systemic Thyroid Hormone Status During Levothyroxine Therapy In Hypothyroidism: A Systematic Review and Meta-Analysis. *J Clin Endocrinol Metab*, still in print.
Ref ID: 37038

202. McCarthy,D., Matz,B., Wright,J. & Moore,L. (2018). Investigation of the HotDog patient warming system: detection of thermal gradients. *J Small Anim Pract*, 59: 298-304.
Ref ID: 36900

203. McGovern,P.D., Albrecht,M., Belani,K.G., Nachtsheim,C., Partington,P.F., Carluke,I. & Reed,M.R. (2011). Forced-air warming and ultra-clean ventilation do not mix: an investigation of theatre ventilation, patient warming and joint replacement infection in orthopaedics. *J Bone Joint Surg Br*, 93: 1537-1544.
Ref ID: 36162

204. McGrory,B.J. (2018). Letter to the Editor on "Hypothermia in Total Joint Arthroplasty: A Wake-Up Call". *J Arthroplasty*, still in print.
Ref ID: 36930

205. Meding,J.B., Reddleman,K., Keating,M.E., Klay,A., Ritter,M.A., Faris,P.M. & Berend,M.E. (2003). Total knee replacement in patients with diabetes mellitus. *Clin Orthop Relat Res*, 416: 208-216.
Ref ID: 36946

206. Meehan,J., Jamali,A.A. & Nguyen,H. (2009). Prophylactic antibiotics in hip and knee arthroplasty. *J Bone Joint Surg Am*, 91: 2480-2490.
Ref ID: 36913

207. Melling,A.C., Ali,B., Scott,E.M. & Leaper,D.J. (2001). Effects of preoperative warming on the incidence of wound infection after clean surgery: a randomised controlled trial. *Lancet*, 358: 876-880.
Ref ID: 36275

BAIR HUGGER REFERENCE LIST
(continued)

208. Menendez,M.E., Ring,D. & Bateman,B.T. (2015). Preoperative opioid misuse is associated with increased morbidity and mortality after elective orthopaedic surgery. *Clin Orthop Relat Res*, 473: 2402-2412.
Ref ID: 36888

209. Merli,G.J. & Groce,J.B. (2010). Pharmacological and clinical differences between low-molecular-weight heparins: implications for prescribing practice and therapeutic interchange. *Pharm Ther*, 35: 95-105.
Ref ID: 36728

210. Misteli,H., Weber,W.P., Reck,S., Rosenthal,R., Zwahlen,M., Fueglistaler,P., Bolli,M.K., Oertli,D., Widmer,A.F. & Marti,W.R. (2009). Surgical glove perforation and the risk of surgical site infection. *Arch Surg*, 144: 553-558.
Ref ID: 36593

211. Moeckel,B., Huo,M.H., Salvati,E.A. & Pellicci,P.M. (1993). Total hip arthroplasty in patients with diabetes mellitus. *J Arthroplasty*, 8: 279-284.
Ref ID: 36467

212. Montes,L.F. & Wilborn,W.H. (1969). Location of bacterial skin flora. *Br J Dermatol*, 81 (suppl 1): 23-26.
Ref ID: 36991

213. Montes,L.F. & Wilborn,W.H. (1970). Anatomical location of normal skin flora. *Arch Dermatol*, 101: 145-159.
Ref ID: 36994

214. Moretti,B., Larocca,A.M., Napoli,C., Martinelli,D., Paolillo,L., Cassano,M., Notarnicola,A., Moretti,L. & Pesce,V. (2009). Active warming systems to maintain perioperative normothermia in hip replacement surgery: a therapeutic aid or a vector of infection? *J Hosp Infect*, 73: 58-63.
Ref ID: 36218

215. Morgenstern,M., Erichsen,C., Hackl,S., Mily,J., Militz,M., Friederichs,J., Hungerer,S., Buhren,V., Moriarty,T.F. & et al (2016). Antibiotic Resistance of Commensal Staphylococcus aureus and Coagulase-Negative Staphylococci in an International Cohort of Surgeons: A Prospective Point-Prevalence Study. *PloS One*, 11: e0148437.
Ref ID: 36605

216. Moucha,C.S., Clyburn,T., Evans,R.P. & Prokuski,L. (2011). Modifiable risk factors for surgical site infection. *J Bone Joint Surg Am*, 93: 398-404.
Ref ID: 36914

BAIR HUGGER REFERENCE LIST
(continued)

217. Muller,C.S., Hubner,W., Thieme-Ruffing,S., Pfohler,C., Vogt,T., Volk,T., Gartner,B.C. & Bialas,P. (2017). Pre- and perioperative aspects of dermatosurgery. *J Dtsch Dermatol Ges*, 15: 117-146.
Ref ID: 36666

218. Myers,E., O'Grady,P. & Dolan,A.M. (2004). The influence of preclinical anaemia on outcome following total hip replacement. *Arch Orthop Trauma Surg*, 124: 699-701.
Ref ID: 36863

219. Namba,R.S., Paxton,L., Fithian,D.C. & Stone,M.L. (2005). Obesity and perioperative morbidity in total hip and total knee arthroplasty patients. *J Arthroplasty*, 20 (Suppl 3): 46-50.
Ref ID: 36935

220. Namba,R.S., Inacio,M.C. & Paxton,E.W. (2012). Risk factors associated with surgical site infection in 30,491 primary total hip replacements. *J Bone Joint Surg Br*, 94: 1330-1338.
Ref ID: 36936

221. Namba,R.S., Inacio,M.C. & Paxton,E.W. (2013). Risk factors associated with deep surgical site infections after primary total knee arthroplasty: an analysis of 56,216 knees. *J Bone Joint Surg Am*, 95: 775-782.
Ref ID: 36909

222. Namba,R.S., Inacio,M.C., Pratt,N.L., Graves,S.E., Roughead,E.E., Craig Cheetham,T. & Paxton,E.W. (2016). Postoperative opioid use as an early indication of total hip arthroplasty failure. *Acta Orthop*, 87 (suppl 1): 37-43.
Ref ID: 36891

223. Namba,R.S., Inacio,M.C.S., Pratt,N.L., Graves,S.E., Roughead,E.E. & Paxton,E.W. (2018). Persistent opioid use following total knee arthroplasty: A signal for close surveillance. *J Arthroplasty* , 33: 331-336.
Ref ID: 36890

224. Napolitano,L.M. (2006). Decolonization of the skin of the patient and surgeon. *Surg Infect (Larchmt)*, 7 (suppl 3): S3-S15.
Ref ID: 36185

225. National Research Council of the National Academies (2011). *Reference Manual on Scientific Evidence* (3rd Edn). Washington, DC: The National Academies Press.
Ref ID: 37023

BAIR HUGGER REFERENCE LIST
(continued)

226. Nunez,M., Lozano,L., Nunez,E., Sastre,S., Luis Del Val,J. & Suso,S. (2011). Good quality of life in severely obese total knee replacement patients: a case-control study. *Obes Surg*, 21: 1203-1208.
Ref ID: 36934

227. Odunayo,A., Dodam,J.R., Kerl,M.E. & DeClue,A.E. (2010). Immunomodulatory effects of opioids. *J Vet Emerg Crit Care (San Antonio)*, 20: 376-385.
Ref ID: 36998

228. Oguz,R., Diab-Elschahawi,M., Berger,J., Auer,N., Chiari,A., Assadian,O. & Kimberger,O. (2017). Airborne bacterial contamination during orthopedic surgery: A randomized controlled pilot trial. *J Clin Anesth*, 38: 160-164.
Ref ID: 36210

229. Olsen,M.A., Nepple,J.J., Riew,K.D., Lenke,L.G., Bridwell,K.H., Mayfield,J. & Fraser,V.J. (2008). Risk factors for surgical site infection following orthopaedic spinal operations. *J Bone Joint Surg Am*, 90: 62-69.
Ref ID: 36169

230. Ostrander,R.V., Botte,M.J. & Brage,M.E. (2005). Efficacy of surgical preparation solutions in foot and ankle surgery. *J Bone Joint Surg Am*, 87: 980-985.
Ref ID: 36187

231. Palace,M.R. (2017). Perioperative management of thyroid dysfunction. *Health Serv Insights*, 10: 1-5.
Ref ID: 37033

232. Papagelopoulos,P.J., Idusuyi,O.B., Wallrichs,S.L. & Morrey,B.F. (1996). Long term outcome and survivorship analysis of primary total knee arthroplasty in patients with diabetes mellitus. *Clin Orthop Relat Res*, 330: 124-132.
Ref ID: 36468

233. Papas,P.V., Congiusta,D., Scuderi,G.R. & Cushner,F.D. (2018). A modern appproach to preventing prosthetic joint infections. *J Knee Surg*, 31: 610-617.
Ref ID: 36907

234. Parsons,H.M. (1974). What Happened at Hawthorne?: New evidence suggests the Hawthorne effect resulted from operant reinforcement contingencies. *Science*, 183: 922-932.
Ref ID: 36269

235. Parvizi,J., Gehrke,T. & Chen,A.F. (2013). Proceedings of the International Consensus on Periprosthetic Joint Infection. *Bone Joint J*, 95-B: 1450-1452.
Ref ID: 36920

BAIR HUGGER REFERENCE LIST
(continued)

236. Pasala,S., Barr,T. & Messaoudi,I. (2015). Impact of alcohol abuse on the adaptive immune system. *Alcohol Res*, 37: 185-197.
Ref ID: 37052

237. Patel,V.P., Walsh,M., Sehgal,B., Preston,C., DeWal,H. & Di Cesare,P.E. (2007). Factors associated with prolonged wound drainage after primary total hip and knee arthroplasty. *J Bone Joint Surg Am*, 89: 33-38.
Ref ID: 36216

238. Paulsen,J., Askim,A., Mohus,R.M., Mehl,A., Dewan,A., Solligard,E., Damas,J.K. & Asvold,B.O. (2017). Associations of obesity and lifestyle with the risk and mortality of bloodstream infection in a general population: a 15-year follow-up of 64 027 individuals in the HUNT Study. *Int J Epidemiol*, 46: 1573-1581.
Ref ID: 36687

239. Paxton,E.W., Inacio,M.C., Singh,J.A., Love,R., Bini,S.A. & Namba,R.S. (2015). Are There Modifiable Risk Factors for Hospital Readmission After Total Hip Arthroplasty in a US Healthcare System? *Clin Orthop Relat Res*, 473: 3446-3455.
Ref ID: 37034

240. Payne,K.D. & Hall,R.G., II (2014). Dosing of antibacterial agents in obese adults: does one size fit all? *Expert Rev Anti Infect ther*, 12: 829-854.
Ref ID: 36526

241. Pedersen,A.B., Mehnert,F., Johnsen,S.P. & Sorensen,H.T. (2010). Risk of revision of a total hip replacement in patients with diabetes mellitus: a population-based follow up study. *J Bone Joint Surg Br*, 92: 929-934.
Ref ID: 36947

242. Peel,T.N., Dowsey,M.M., Daffy,J.R., Stanley,P.A., Choong,P.F. & Buising,K.L. (2011). Risk factors for prosthetic hip and knee infections according to arthroplasty site. *J Hosp Infect*, 79: 129-133.
Ref ID: 36442

243. Peersman,G., Laskin,R., Davis,J. & Peterson,M. (2001). Infection in total knee replacement: a retrospective review of 6489 total knee replacements. *Clin Orthop Relat Res*, 392 (Nov): 15-23.
Ref ID: 36206

244. Perl,T., Peichl,L.H., Reyntjens,K., Deblaere,I., Zaballos,J.M. & Brauer,A. (2014). Efficacy of a novel prewarming system in the prevention of perioperative hypothermia. A prospective, randomized, multicenter study. *Minerva Anestesiol*, 80: 436-443.
Ref ID: 37035

BAIR HUGGER REFERENCE LIST
(continued)

245. Pevzner,L., Swank,M., Krepel,C., Wing,D.A., Chan,K. & Edmiston,C.E., Jr. (2011). Effects of maternal obesity on tissue concentrations of prophylactic cefazolin during cesarean delivery. *Obstet Gynecol*, 117: 877-882.
Ref ID: 36525

246. Poole,C. (1987). Confidence intervals exclude nothing. *Am J Public Health*, 77: 492-493.
Ref ID: 36223

247. Porta,M. (2014). *A Dictionary of Epidemiology* (6th Edn). New York: Oxford University Press.
Ref ID: 36259

248. Pulido,L., Ghanem,E., Joshi,A., Purtill,J.J. & Parvizi,J. (2008). Periprosthetic joint infection: the incidence, timing, and predisposing factors. *Clin Orthop Relat Res*, 466: 1710-1715.
Ref ID: 36444

249. Qadan,M., Akca,O., Mahid,S.S., Hornung,C.A. & Polk,H.C., Jr. (2009). Perioperative supplemental oxygen therapy and surgical site infection: a meta-analysis of randomized controlled trials. *Arch Surg*, 144: 359-366.
Ref ID: 36553

250. Rajagopalan,S., Mascha,E., Na,J. & Sessler,D.I. (2008). The effects of mild perioperative hypothermia on blood loss and transfusion requirement. *Anesthesiology*, 108: 71-77.
Ref ID: 37008

251. Rajaraman,P. & Samet,J.M. (2005). Quality Control and Good Epidemiological Practice. In: Ahrens,W. & Pigeot,I. (Eds.), *Handbook of Epidemiology*, pp. 503-556. New York: Springer. 556 pp.
Ref ID: 37022

252. Ranario,J.S., Watkins,B.F. & Shimizu,I. (2018). Rate of surgical site infections with new protocol of prophylactic antibiotic use in dermatologic surgery. *Dermatol Surg*, 44: 304-306.
Ref ID: 36665

253. Rao,N., Cannella,B., Crossett,L.S., Yates,A.J., Jr. & McGough,R., III (2008). A preoperative decolonization protocol for staphylococcus aureus prevents orthopaedic infections. *Clin Orthop Relat Res*, 466: 1343-1348.
Ref ID: 36579

BAIR HUGGER REFERENCE LIST
(continued)

254. Refaie,R., Jameson,S. & Reed,M. (2015). Prevention of periprosthetic joint infection. *J Trauma Ortho*, 3: 50-52.
Ref ID: 36271

255. Refaie,R., Rushton,P., McGovern,P., Thompson,D., Serrano-Pedraza,I., Rankin,K.S. & Reed,M. (2017). The effect of operating lights on laminar flow. An experimental study using neutrally buoyant helium bubbles. *Bone Joint J*, 99-B: 1061-1066.
Ref ID: 36385

256. Renaud,A., Lavigne,M. & Vendittoli,P.A. (2012). Periprosthetic joint infections at a teaching hospital in 1990-2007. *Can J Surg*, 55: 394-400.
Ref ID: 36446

257. Reynolds,L., Beckmann,J. & Kurz,A. (2008). Perioperative complications of hypothermia. *Best Pract Res Clin Anaesthesiol*, 22: 645-657.
Ref ID: 37009

258. Reyntjens,K., Dejongh,K., Monstrez,S., Struys,M. & Mortier,E. (2008). Peroperative temperature management. Comparison of a forced air warming device and a dynamic air mattress device in plastic surgery: 3AP1-2. *Eur J Anaesthesiol*, 25 (suppl 44): 25.
Ref ID: 37040

259. Roberts,F.J., Geere,I.W. & Coldman,A. (1991). A three-year study of positive blood cultures, with emphasis on prognosis. *Rev Infect Dis*, 13: 34-46.
Ref ID: 36660

260. Rogers,B.A., Cowie,A., Alcock,C. & Rosson,J.W. (2008). Identification and treatment of anaemia in patients awaiting hip replacement. *Ann R Coll Surg Engl*, 90: 504-507.
Ref ID: 36864

261. Rohrich,R.J. (2011). Current concepts in wound healing: update 2011. *Plast Reconstr Surg*, 127 (suppl 1): 1S-2S.
Ref ID: 36916

262. Rollins,K.E., Varadhan,K.K., Dhatariya,K. & Lobo,D.N. (2016). Systematic review of the impact of HbA1c on outcomes following surgery in patients with diabetes mellitus. *Clin Nutr*, 35: 308-316.
Ref ID: 36977

263. Romano,P.S., Roos,L.L. & Jollis,J.G. (1993). Adapting a clinical comorbidity index for use with ICD-9-CM administrative data: differing perspectives. *J Clin Epidemiol*, 46: 1075-1079.
Ref ID: 36978

BAIR HUGGER REFERENCE LIST
(continued)

264. Rosengren,H. (2012). An update on antibiotic prophylaxis in dermatological surgery. *Curr Derm Rep*, 1: 55-63.
Ref ID: 36667

265. Rossi,A.M. & Mariwalla,K. (2012). Prophylactic and empiric use of antibiotics in dermatologic surgery: a review of the literature and practical considerations. *Dermatol Surg*, 38: 1898-1921.
Ref ID: 36671

266. Rothman,K.J. (1995). Causes. *Am J Epidemiol*, 141: 90-95.
Ref ID: 36238

267. Rothman,K.J. & Greenland,S. (2005). Causation and causal inference in epidemiology. *Am J Pub Health*, 95 (suppl 1): S144-S150.
Ref ID: 30881

268. Rozell,J.C., Courtney,P.M., Dattilo,J.R., Wu,C.H. & Lee,G.C. (2017). Preoperative opiate use independently predicts narcotic consumption and complications after total joint arthroplasty. *J Arthroplasty*, 32: 2658-2662.
Ref ID: 36893

269. Rupp,M.E. & Hamer,K.E. (1998). Effect of subinhibitory concentrations of vancomycin, cefazolin, ofloxacin, L-ofloxacin and D-ofloxacin on adherence to intravascular catheters and biofilm formation by Staphylococcus epidermidis. *J Antimicrob Chemother*, 41: 155-161.
Ref ID: 37026

270. Rupp,M.E. (2014). Clinical characteristics of infections in humans due to Staphylococcus epidermidis. *Methods Mol Biol*, 1106: 1-16.
Ref ID: 36539

271. Sabetta,J.B. & Zitelli,J.A. (1987). The incidence of bacteremia during skin surgery. *Arch Dermatol*, 123: 213-215.
Ref ID: 36659

272. Sacerdote,P. (2006). Opioids and the immune system. *Palliat Med*, 20 (suppl 1): s9-s15.
Ref ID: 36973

273. Sacerdote,P. (2008). Opioid-induced immunosuppression. *Curr Opin Support Palliat Care*, 2: 14-18.
Ref ID: 36999

274. Salassa,T.E. & Swiontkowski,M.F. (2014). Surgical attire and the operating room: role in infection prevention. *J Bone Joint Surg Am*, 96: 1485-1492.
Ref ID: 36906

BAIR HUGGER REFERENCE LIST
(continued)

275. Saleh,E., McClelland,D.B., Hay,A., Semple,D. & Walsh,T.S. (2007). Prevalence of anaemia before major joint arthroplasty and the potential impact of preoperative investigation and correction on perioperative blood transfusions. *Br J Anaesth*, 99: 801-808.
Ref ID: 36865

276. Saleh,K., Olson,M., Resig,S., Bershadsky,B., Kuskowski,M., Gioe,T., Robinson,H. & McElfresh,E. (2002). Predictors of wound infection in hip and knee joint replacement: results from a 20 year surveillance program. *J Orthop Res*, 20: 506-515.
Ref ID: 36438

277. Samet,J.M. (2016). Epidemiology and the Tobacco Epidemic: How Research on Tobacco and Health Shaped Epidemiology. *Am J Epidemiol*, 183: 394-402.
Ref ID: 36333

278. Schmied,H., Kurz,A., Sessler,D.I., Kozek,S. & Reiter,A. (1996). Mild hypothermia increases blood loss and transfusion requirements during total hip arthroplasty. *Lancet*, 347: 289-292.
Ref ID: 37010

279. Schmitz,F.J., Fluit,A.C., Gondolf,M., Beyrau,F., Lindenlauf,E., Verhoef,J., Heins,H.P. & Jones,M.E. (1999). The prevalence of aminoglycoside resistance and corresponding resistance genes in clinical isolates of staphylococci from 19 European hospitals. *J Antimicrob Chemother*, 43: 253-259.
Ref ID: 36257

280. Schoenfeld,P.S., Myers,J.W., Myers,L. & LaRocque,J.C. (1995). Suppression of cell-mediated immunity in hypothyroidism. *South Med J*, 88: 347-349.
Ref ID: 36855

281. Scholten,R., Leijtens,B., Kremers,K., Snoeck,M. & Koeter,S. (2018). The incidence of mild hypothermia after total knee or hip arthroplasty: A study of 2600 patients. *J Orthop*, 15: 408-411.
Ref ID: 36932

282. Schweizer,M.L., Chiang,H.Y., Septimus,E., Moody,J., Braun,B., Hafner,J. & et al (2015). Association of a bundled intervention with surgical site infections among patients undergoing cardiac, hip, or knee surgery. *J Am Med Assoc*, 313: 2162-2171.
Ref ID: 36598

283. Scott,A.V., Stonemetz,J.L., Wasey,J.O., Johnson,D.J., Rivers,R.J., Koch,C.G. & Frank,S.M. (2015). Compliance with Surgical Care Improvement Project for Body Temperature Management (SCIP Inf-10) Is Associated with Improved Clinical Outcomes. *Anesthesiology*, 123: 116-125.
Ref ID: 37017

BAIR HUGGER REFERENCE LIST
(continued)

284. Scuderi,G.R. (2018). Avoiding postoperative wound complications in total joint arthroplasty. *J Arthroplasty*, still in print.
Ref ID: 36908

285. Segawa,H., Tsukayama,D., Kyle,R.F., Becker,D.A. & Gustilo,R.B. (1999). Infection after total knee arthroplasty. A retrospective study of the treatment of eighty-one infections. *J Bone Joint Surg*, 81: 1434-1445.
Ref ID: 36263

286. Sehjal,R., Bakti,N. & Goddard,R. (2017). Effect of an anaesthetic screening drape on vertical laminar airflow. *J Hosp Infect*, 96: 331-335.
Ref ID: 37036

287. Shohat,N., Goswami,K., Tarabichi,M., Sterbis,E., Tan,T.L. & Parvizi,J. (2018). All patients should be screened for diabetes before total joint arthroplasty. *J Arthroplasty*, 33: 2057-2061.
Ref ID: 36950

288. Sikka,R.S. & Prielipp,R.C. (2014). Forced air warming devices in orthopaedics: a focused review of the literature. *J Bone Joint Surg Am*, 96: e200-1-e200-7.
Ref ID: 36278

289. Simpson,J.B., Thomas,V., Ismaily,S.K., Muradov,P.I., Noble,P.C. & Incavo,S.J. (2018). Hypothermia in total joint arthroplasty: A Wake-Up Call. *J Arthroplasty*, 33: 1012-1018.
Ref ID: 36931

290. Singh,S., Reddy,S. & Shrivastava,R. (2017). Does laminar airflow make a difference to the infection rates for lower limb arthroplasty: a study using the National Joint Registry and local surgical site infection data for two hospitals with and without laminar airflow. *Eur J Orthop Surg Traumatol*, 27: 261-265.
Ref ID: 36211

291. Smith,R.L., Bohl,J.K., McElearney,S.T., Friel,C.M., Barclay,M.M., Sawyer,R.G. & Foley,E.F. (2004). Wound infection after elective colorectal resection. *Ann Surg*, 239: 599-605.
Ref ID: 36532

292. Sommerstein,R., Ruegg,C., Kohler,P., Bloemberg,G., Kuster,S.P. & Sax,H. (2016). Transmission of mycobacterium chimaera from heater-cooler units during cardiac surgery despite an ultraclean air ventilation system. *Emerg Infect Dis*, 22: 1008-1013.
Ref ID: 36346

BAIR HUGGER REFERENCE LIST
(continued)

293. Song,Z., Borgwardt,L., Hoiby,N., Wu,H., Sorensen,T.S. & Borgwardt,A. (2013). Prosthesis infections after orthopedic joint replacement: the possible role of bacterial biofilms. *Orthop Rev (Pavia)*, 5: 65-71.
Ref ID: 36264

294. Soohoo,N.F., Farng,E., Lieberman,J.R., Chambers,L. & Zingmond,D.S. (2010). Factors that predict short-term complication rates after total hip arthroplasty. *Clin Orthop Relat Res*, 468: 2363-2371.
Ref ID: 36968

295. Spagnolo,A.M., Ottria,G., Amicizia,D., Perdelli,F. & Cristina,M.L. (2013). Operating theatre quality and prevention of surgical site infections. *J Prev Med Hyg*, 54: 131-137.
Ref ID: 36349

296. Spahn,D.R. (2010). Anemia and patient blood management in hip and knee surgery: a systematic review of the literature. *Anesthesiology*, 113: 482-495.
Ref ID: 36866

297. Speller,D.C., Raghunath,D., Stephens,M., Viant,A.C., Reeves,D.S., Wilkinson,P.J., Broughall,J.M. & Holt,H.A. (1976). Epidemic infection by a gentamicin-resistant Staphylococcus aureus in three hospitals. *Lancet*, 307: 464-466.
Ref ID: 36255

298. Spelman,D.W., Weinmann,A. & Spicer,W.J. (1993). Endocarditis following skin procedures. *J Infect*, 26: 185-189.
Ref ID: 36669

299. Spelman,D.W., Russo,P., Harrington,G., Davis,B.B., Rabinov,M., Smith,J.A., Spicer,W.J. & Esmore,D. (2000). Risk factors for surgical wound infection and bacteraemia following coronary artery bypass surgery. *Aust N Z J Surg*, 70: 47-51.
Ref ID: 36686

300. Spencer,C.A. (1988). Clinical utility and cost-effectiveness of sensitive thyrotropin assays in ambulatory and hospitalized patients. *Mayo Clin Proc*, 63: 1214-1222.
Ref ID: 37041

301. Sporer,S.M., Rogers,T. & Abella,L. (2016). Methicillin-Resistant and Methicillin-Sensitive Staphylococcus aureus Screening and Decolonization to Reduce Surgical Site Infection in Elective Total Joint Arthroplasty. *J Arthroplasty*, 31: 144-147.
Ref ID: 36878

302. Sprowson,A., Symes,T., Khan,S.K., Oswald,T. & Reed,M.R. (2013). Changing antibiotic prophylaxis for primary joint arthroplasty affects postoperative complication rates and bacterial spectrum. *Surgeon*, 11: 20-24.
Ref ID: 36276

BAIR HUGGER REFERENCE LIST
(continued)

303. Stenehjem,E., Crispell,E.K., Rimland,D., Farley,M.M. & Satola,S.W. (2015). Longitudinal evaluation of clinical and colonization methicillin-resistant Staphylococcus aureus isolates among veterans. *Infect Control Hosp Epidemiol*, 36: 587-589.
Ref ID: 36877

304. Stern,S.H. & Insall,J.N. (1990). Total knee arthroplasty in obese patients. *J Bone Joint Surg Am*, 72: 1400-1404.
Ref ID: 36469

305. Stocks,G.W., Self,S.D., Thompson,B., Adame,X.A. & O'Connor,D.P. (2010). Predicting bacterial populations based on airborne particulates: A study performed in nonlaminar flow operating rooms during joint arthroplasty surgery. *Am J Infect Control*, 38: 199-204.
Ref ID: 36544

306. Storrs,M.J., Courvalin,P. & Foster,T.J. (1988). Genetic analysis of gentamicin resistance in methicillin- and gentamicin-resistant strains of Staphylococcus aureus isolated in Dublin hospitals. *Antimicrob Agents Chemother*, 32: 1174-1181.
Ref ID: 36256

307. Stryker,L.S., Abdel,M.P., Morrey,M.E., Morrow,M.M., Kor,D.J. & Morrey,B.F. (2013). Elevated postoperative blood glucose and preoperative hemoglobin A1C are associated with increased wound complications following total joint arthroplasty. *J Bone Joint Surg Am*, 95: 808-814.
Ref ID: 36944

308. Sun,Z., Honar,H., Sessler,D.I., Dalton,J.E., Yang,D., Panjasawatwong,K., Deroee,A.F. & et al (2015). Intraoperative core temperature patterns, transfusion requirement, and hospital duration in patients warmed with forced air. *Anesthesiology*, 122: 276-285.
Ref ID: 37015

309. Sundaram,V., Kaung,A., Rajaram,A., Lu,S.C., Tran,T.T., Nissen,N.N., Klein,A.S., Jalan,R., Charlton,M.R. & Jeon,C.Y. (2015). Obesity is independently associated with infection in hospitalised patients with end-stage liver disease. *Aliment Pharmacol Ther*, 42: 1271-1280.
Ref ID: 36688

310. Swenson,B.R., Hedrick,T.L., Metzger,R., Bonatti,H., Pruett,T.L. & Sawyer,R.G. (2009). Effects of preoperative skin preparation on postoperative wound infection rates: a prospective study of 3 skin preparation protocols. *Infect Control Hosp Epidemiol*, 30: 964-971.
Ref ID: 36190

BAIR HUGGER REFERENCE LIST
(continued)

311. Szabo,G. & Mandrekar,P. (2009). A recent perspective on alcohol, immunity, and host defense. *Alcohol Clin Exp Res*, 33: 220-232.
Ref ID: 33577

312. Szabo,G. & Saha,B. (2015). Alcohol's effect on host defense. *Alcohol Res*, 37: 159-170.
Ref ID: 37047

313. Tan,T.L., Kheir,M.M. & Chen,A.F. (2016). Who is at Risk for Periprosthetic Joint Infection? In: Kendoff,D., Morgan-Jones,R. & Haddad,F.S. (Eds.), *Periprosthetic Joint Infections. Changing Paradigms*, pp. 61-75. Swizerland: Springer. 75 pp.
Ref ID: 36966

314. Tan,T.L., Rajeswaran,H., Haddad,S., Shahi,A. & Parvizi,J. (2016). Increased risk of periprosthetic joint infections in patients with hypothyroidism undergoing total joint arthroplasty. *J Arthroplasty*, 31: 868-871.
Ref ID: 36847

315. Tan,T.L., Maltenfort,M.G., Chen,A.F., Shahi,A., Higuera,C.A., Siqueira,M. & Parvizi,J. (2018). Development and evaluation of a preoperative risk calculator for periprosthetic joint infection following total joint arthroplasty. *J Bone Joint Surg Am*, 100: 777-785.
Ref ID: 36970

316. Tanner,J. & Parkinson,H. (2009). *Double Gloving to Reduce Surgical Cross-Infection (Review)* John Wiley & Sons, Ltd, The Cochrane Library.
Ref ID: 36592

317. Tayton,E.R., Frampton,C., Hooper,G.J. & Young,S.W. (2016). The impact of patient and surgical factors on the rate of infection after primary total knee arthroplasty: an analysis of 64,566 joints from the New Zealand Joint Registry. *Bone Joint J*, 98-B: 334-340.
Ref ID: 36220

318. Triantafyllopoulos,G., Stundner,O., Memtsoudis,S. & Poultsides,L.A. (2015). Patient, Surgery, and Hospital Related Risk Factors for Surgical Site Infections following Total Hip Arthroplasty. *Scientific WorldJournal*, 2015.
Ref ID: 36448

319. Tsang,S.T. & Gaston,P. (2013). Adverse peri-operative outcomes following elective total hip replacement in diabetes mellitus: a systematic review and meta-analysis of cohort studies. *Bone Joint J*, 95-B: 1474-1479.
Ref ID: 36477

BAIR HUGGER REFERENCE LIST
(continued)

320. Tumia,N. & Ashcroft,G.P. (2002). Convection warmers--a possible source of contamination in laminar airflow operating theatres? *J Hosp Infect*, 52: 171-174.
Ref ID: 36171

321. Turpie,A.G., Lassen,M.R., Davidson,B.L., Bauer,K.A., Gent,M., Kwong,L.M., Cushner,F.D., Lotke,P.A. & etal (2009). Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty (RECORD4): a randomised trial. *Lancet*, 373: 1673-1680.
Ref ID: 36176

322. Tustanowski,J. (2009). Effect of dressing choice on outcomes after hip and knee arthroplasty: a literature review. *J Wound Care*, 18: 449-450.
Ref ID: 36195

323. van Ingen,J., Kohl,T.A., Kranzer,K., Hasse,B., Keller,P.M., Katarzyna Szafranska,A., Hillemann,D., Chand,M., Schreiber,P.W., Sommerstein,R., Berger,C. & et al (2017). Global outbreak of severe Mycobacterium chimaera disease after cardiac surgery: a molecular epidemiological study. *Lancet Infect Dis*, 17: 1033-1041.
Ref ID: 36390

324. van Kralingen,S., Taks,M., Diepstraten,J., van de Garde,E.M., van Dongen,E.P., Wiezer,M.J., van Ramshorst,B. & Vlaminckx,B. (2011). Pharmacokinetics and protein binding of cefazolin in morbidly obese patients. *Eur J Clin Pharmacol*, 67: 985-992.
Ref ID: 36534

325. van Rijen,M., Bonten,M., Wenzel,R. & Kluytmans,J. (2011). Mupirocin ointment for preventing Staphylococcus aureus infections in nasal carriers. *Cochrane Database Syst Rev*, 8 (ID: CD006216): 1-28.
Ref ID: 36191

326. van Rijen,M.M., Bonten,M., Wenzel,R.P. & Kluytmans,J.A. (2008). Intranasal mupirocin for reduction of Staphylococcus aureus infections in surgical patients with nasal carriage: a systematic review. *J Antimicrob Chemother*, 61: 254-261.
Ref ID: 36189

327. Verhoeven,P.O., Berthelot,P., Chapelle,C., Gagnaire,J., Grattard,F., Pozzetto,B., Farizon,F., Lucht,F. & Botelho-Nevers,E. (2013). Letter to the editor: Staphylococcus aureus screening and decolonization in orthopaedic surgery and reduction of surgical site infections. *Clin Orthop Relat Res*, 471: 3709-3711.
Ref ID: 36896

328. von Eiff,C., Becker,K., Machka,K., Stammer,H. & Peters,G. (2001). Nasal carriage as a source of staphylococcus aureus bacteremia. Study Group. *N Engl J Med*, 344: 11-16.
Ref ID: 36895

BAIR HUGGER REFERENCE LIST
(continued)

329. Waisbren,E., Rosen,H., Bader,A.M., Lipsitz,S.R., Rogers,S.O., Jr. & Eriksson,E. (2010). Percent body fat and prediction of surgical site infection. *J Am Coll Surg*, 210: 381-389.
Ref ID: 37027

330. Wang,H.E., Griffin,R., Judd,S., Shapiro,N.I. & Safford,M.M. (2013). Obesity and risk of sepsis: a population-based cohort study. *Obesity (Silver Spring)*, 21: E762-E769.
Ref ID: 36689

331. Wang,Z., Anderson,F.A., Jr., Ward,M. & Bhattacharyya,T. (2014). Surgical site infections and other postoperative complications following prophylactic anticoagulation in total joint arthroplasty. *PloS One*, 9: e91755.
Ref ID: 36449

332. Wawer,A.A., Jennings,A. & Fairweather-Tait,S.J. (2018). Iron status in the elderly: A review of recent evidence. *Mech Ageing Dev*, 175: 55-73.
Ref ID: 37012

333. Weed,D.L. (1986). On the logic of causal inference. *Am J Epidemiol*, 123: 965-979.
Ref ID: 36239

334. Weick,J., Bawa,H., Dirschl,D.R. & Luu,H.H. (2018). Preoperative opioid use is associated with higher readmission and revision rates in total knee and total hip arthroplasty. *J Bone Joint Surg Am*, 100: 1171-1176.
Ref ID: 36885

335. Weiser,M.C. & Moucha,C.S. (2015). The Current State of Screening and Decolonization for the Prevention of Staphylococcus aureus Surgical Site Infection. *J Bone Joint Surg Am*, 97: 1449-1458.
Ref ID: 36202

336. Weiser,M.C. & Moucha,C.S. (2018). Operating-room airflow technology and infection prevention. *J Bone Joint Surg Am*, 100: 795-804.
Ref ID: 37032

337. Wenzel,R.P. & Perl,T.M. (1995). The significance of nasal carriage of Staphylococcus aureus and the incidence of postoperative wound infection. *J Hosp Infect*, 31: 13-24.
Ref ID: 36212

338. Wenzel,R.P. (2010). Minimizing surgical-site infections. *N Engl J Med*, 362: 75-77.
Ref ID: 36194

339. Wertheim,H.F., Melles,D.C., Vos,M.C., van Leeuwen,W., van Belkum,A., Verbrugh,H.A. & Nouwen,J.L. (2005). The role of nasal carriage in Staphylococcus aureus infections. *Lancet Infect Dis*, 5: 751-762.
Ref ID: 28351

BAIR HUGGER REFERENCE LIST

(continued)

340. Wick,E.C., Hirose,K., Shore,A.D., Clark,J.M., Gearhart,S.L., Efron,J. & Makary,M.A. (2011). Surgical site infections and cost in obese patients undergoing colorectal surgery. *Arch Surg*, 146: 1068-1072.
Ref ID: 36531

341. Wiley,A.M. & Ha'eri,G.B. (1979). Routes of infection. A study of using "tracer particles" in the orthopedic operating room. *Clin Orthop Relat Res*, 139: 150-155.
Ref ID: 37020

342. Winiarsky,R., Barth,P. & Lotke,P. (1998). Total knee arthroplasty in morbidly obese patients. *J Bone Joint Surg Am*, 80: 1770-1774.
Ref ID: 36470

343. Winkler,M., Akca,O., Birkenberg,B., Hetz,H., Scheck,T., Arkilic,C.F., Kabon,B. & etal (2000). Aggressive warming reduces blood loss during hip arthroplasty. *Anesth Analg*, 91: 978-984.
Ref ID: 37016

344. Wong,P.F., Kumar,S., Bohra,A., Whetter,D. & Leaper,D.J. (2007). Randomized clinical trial of perioperative systemic warming in major elective abdominal surgery. *Br J Surg*, 94: 421-426.
Ref ID: 36552

345. Wood,A.M., Moss,C., Keenan,A., Reed,M.R. & Leaper,D.J. (2014). Infection control hazards associated with the use of forced-air warming in operating theatres. *J Hosp Infect*, 88: 132-140.
Ref ID: 36213

346. Workgroup of the American Association of Hip and Knee Surgeons Evidence Based Committee (2018). Obesity and total joint arthroplasty: a literature based review. *J Arthroplasty*, 28 : 714-721.
Ref ID: 36919

347. Wright,J.G., Swiontkowski,M.F. & Heckman,J.D. (2003). Introducing levels of evidence to the journal. *J Bone Joint Surg Am*, 85-A: 1-3.
Ref ID: 36576

348. Wright,T.I., Baddour,L.M., Berbari,E.F., Roenigk,R.K., Phillips,P.K., Jacobs,M.A. & Otley,C.C. (2008). Antibiotic prophylaxis in dermatologic surgery: advisory statement 2008. *J Am Acad Dermatol*, 59: 464-473.
Ref ID: 36662

BAIR HUGGER REFERENCE LIST
(continued)

349. Wymenga,A.B., van Horn,J.R., Theeuwes,A., Muytjens,H.L. & Slooff,T.J. (1992). Perioperative factors associated with septic arthritis after arthroplasty. Prospective multicenter study of 362 knee and 2,651 hip operations. *Acta Orthop Scand*, 63: 665-671.
Ref ID: 36739

350. Xu,C., Guo,H., Wang,Q., Qu,P., Bell,K. & Chen,J. (2018). The interaction of obesity with smoking and with inflammatory arthropathies increases the risk of periprosthetic joint infection: A propensity score-matched study in a Chinese Han Population. *J Hosp Infect*, still in print.
Ref ID: 36874

351. Yokoe,D.S., Anderson,D.J., Berenholtz,S.M., Calfee,D.P., Dubberke,E.R., Ellingson,K.D., Gerding,D.N., Haas,J.P., Kaye,K.S., Klompas,M., Lo,E., Marschall,J., Mermel,L.A. & et al (2014). A compendium of strategies to prevent healthcare-associated infections in acute care hospitals: 2014 updates. *Infect Control Hosp Epidemiol*, 35: 967-977.
Ref ID: 36549

352. Yosipovitch,G., DeVore,A. & Dawn,A. (2007). Obesity and the skin: skin physiology and skin manifestations of obesity. *J Am Acad Dermatol*, 56: 901-916.
Ref ID: 36690

353. Yuan,K. & Chen,H.L. (2013). Obesity and surgical site infections risk in orthopedics: a meta-analysis. *Int J Surg*, 11: 383-388.
Ref ID: 36517

354. Zerr,K.J., Furnary,A.P. & et al (1997). Glucose control lowers the risk of wound infection in diabetics after open heart operations. *Ann Thorac Surg*, 63: 356-361.
Ref ID: 36921

355. Zhu,Y., Zhang,F., Chen,W., Liu,S., Zhang,Q. & Zhang,Y. (2015). Risk factors for periprosthetic joint infection after total joint arthroplasty: a systematic review and meta-analysis. *J Hosp Infect*, 89: 82-89.
Ref ID: 37037

356. Zmistowski,B., Dizdarevic,I., Jacovides,C.L., Radcliff,K.E., Mraovic,B. & Parvizi,J. (2013). Patients with uncontrolled components of metabolic syndrome have increased risk of complications following total joint arthroplasty. *J Arthroplasty*, 28: 904-907.
Ref ID: 37043

357. Zywiel,M.G., Daley,J.A., Delanois,R.E., Naziri,Q., Johnson,A.J. & Mont,M.A. (2011). Advance pre-operative chlorhexidine reduces the incidence of surgical site infections in knee arthroplasty. *Int Orthop*, 35: 1001-1006.
Ref ID: 36911

BAIR HUGGER REFERENCE LIST
(continued)

358. Zywiel,M.G., Stroh,D.A., Lee,S.Y., Bonutti,P.M. & Mont,M.A. (2011). Chronic opioid use prior to total knee arthroplasty. *J Bone Joint Surg Am*, 93: 1988-1993.
Ref ID: 36889

EXHIBIT DX12

TO DECLARATION OF BENJAMIN W. HULSE IN SUPPORT OF DEFENDANTS' MOTION FOR RECONSIDERATION OF THE COURT'S DECEMBER 13, 2017 ORDER ON GENERAL CAUSATION

THE JOURNAL OF BONE & JOINT SURGERY (BR)

Return to theatre following total hip and knee replacement, before and after the introduction of rivaroxaban

A RETROSPECTIVE COHORT STUDY

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Rivaroxaban has been recommended for routine use as a thromboprophylactic agent in patients undergoing lower-limb arthroplasty. However, trials supporting its use have not fully evaluated the risks of wound complications. This study of 1048 total hip/knee replacements records the rates of return to theatre and infection before and after the change from a low molecular weight heparin (tinzaparin) to rivaroxaban as the agent of chemical thromboprophylaxis in patients undergoing lower-limb arthroplasty. During a period of 13 months, 489 consecutive patients undergoing lower-limb arthroplasty received tinzaparin and the next 559 consecutive patients received rivaroxaban as thromboprophylaxis.

Nine patients in the control (tinzaparin) group (1.8%, 95% confidence interval 0.9 to 3.5) returned to theatre with wound complications within 30 days, compared with 22 patients in the rivaroxaban group (3.94%, 95% confidence interval 2.6 to 5.9). This increase was statistically significant ($p = 0.046$). The proportion of patients who returned to theatre and became infected remained similar ($p = 0.10$).

Our study demonstrates the need for further randomised controlled clinical trials to be conducted to assess the safety and efficacy of rivaroxaban in clinical practice, focusing on the surgical complications as well as the potential prevention of venous thromboembolism.

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Rivaroxaban (Xarelto; Bayer Schering Pharma AG, Wuppertal, Germany) is one of the first oral factor Xa inhibitors to be licensed for thromboprophylaxis after total knee and hip replacement surgery. Four large studies conducted by RECORD (The Regulation of Coagulation in Orthopaedic Surgery to Prevent Deep Vein Thrombosis and Pulmonary Embolism) have shown it to be effective in preventing venous thromboembolism compared with enoxaparin (Clexane/Lovenox; Sanofi-Aventis, Frankfurt, Germany).[1-4] These studies were the sole evidence on which the National Institute of Clinical Excellence (NICE)[5] based the approval of rivaroxaban for use as chemical thromboprophylaxis following hip and knee joint replacement in England and Wales. Although these studies demonstrated no significant increase in the rates of major bleeding, concerns have been raised about the lack of data on other potential surgical complications.[6-20] Surgical outcomes such as the rate of wound healing, haematoma formation and drainage were either not included or only addressed as secondary safety outcomes by the RECORD trials. These complications have previously been shown to increase rates of wound infection and subsequent return to theatre.[12,13] Risk factors for developing a wound complication and/or infection after a total hip (THR) or knee replacement (TKR) include thromboprophylaxis, immunosuppressive therapy, prolonged wound drainage, obesity, diabetes mellitus, hypothyroidism, renal failure and previous open surgical procedures.[12,13]

Following concerns raised by an author from the RECORD 4 group,[11] this study aimed to report the effects of rivaroxaban on wound complications, infections and return to theatre in patients undergoing THR and TKR.

Patients and Methods

Between February 2009 and February 2010, all the patients who underwent a THR or TKR at our hospital and returned to theatre with a wound-related complication within 30 days of their operation were included in the study. The study period of 13 months included six months prior to and seven months following the introduction of rivaroxaban as the agent of choice for chemical thromboprophylaxis.

Group 1 comprised patients who had their primary operation between 1 February 2009 and 31 July 2009 (six months). These patients

Table I. Demographics and risk factors for wound complications in return to theatre patients in the two groups

	Group 1 (tinzaparin) (n = 9)	Group 2 (rivaroxaban) (n = 22)	Statistical difference between groups 1 and 2
Gender			
M:F	5:4	8:14	0.43†
Operation ratio (TKR:THR)*	1:8	6:16	0.64†
Mean age in years (range)	67 (44 to 81)	64 (39 to 86)	0.93
Body mass index (kg/m²)(range)	31 (26 to 36)	31 (23 to 41)	1.00‡
Chronic renal failure (%)	5 (*55*)	7 (*30*)	0.25†
Diabetes (%)	1 (*11*)	2 (*9*)	1.00†
Hypothyroidism (%)	1 (*11*)	3 (*13*)	1.00†
Immunosuppressive medication (%)	0 (*0*)	1 (*4*)	1.00†
Antithrombotic medication (%)	3 (*33*)	7 (*30*)	1.00†

* TKR, total knee replacement; THR, total hip replacement

† Fisher's exact text for categorical data

‡ *t*-test for continuous data

received tinzaparin (Innohep; LEO Pharma A/S, Ballerup, Denmark) (4500 U subcutaneously, once daily) as thromboprophylaxis from day one post-operatively for 28 days, in accordance with the hospital protocol, which was based on the NICE guidelines.

Group 2 had their primary operation between 1 August 2009 and 28 February 2010 (seven months). They received rivaroxaban (10 mg orally, once daily) as thromboprophylaxis from day one post-operatively in accordance with the new hospital protocol, which reflects the latest guidance from NICE. THRs received prophylaxis for 28 days and TKRs for 14 days.

Patients in both of the groups also wore thromboembolic deterrent stockings for six weeks after surgery, received the same single intravenous dose of prophylactic antibiotics, and were encouraged to mobilise early in the post-operative period. No drains were used at the operation in either group.

Theatre logs from the study period were analysed to identify all patients who had returned to theatre within 30 days of the operation. The hospital case notes were analysed to record demographics and relevant comorbidities that might have contributed as risk factors for delayed wound healing, post-operative bleeding or wound infection (Table I).

Patients were excluded from the return to theatre subanalysis groups if the indication for this was not related to the wound. In group 1, one patient was excluded because of dislocation. In group 2, one patient was excluded because of wound dehiscence after a fall at home, and two were excluded because of dislocation (Fig. 1).

Return to theatre for a wound-related complication was defined as returning to theatre for open irrigation and debridement of a wound within 30 days of the operation. The indication for surgical management of wound problems remained unchanged during the period of the study and was at the clinical discretion of the nine consultant surgeons involved. Indications for return to theatre included clinical signs of wound infection and/or haematoma and raised inflammatory blood markers (including rising trends in CRP, ESR and white cell count). As this study was not a prospective trial, fixed criteria and protocols for indications for return to theatre could not be used. Clinical signs of infection and rising inflammatory markers informed the decisions of the consultant surgeons involved. All the patients who returned to theatre with wound complications had microbiological specimens taken (fluid and tissues) according to departmental protocol. Standard sampling techniques were used, with five samples taken and sterile instruments used for each. The bacterial culture results were retrieved from the hospital laboratory database. The wound was considered deeply infected if the primary samples taken from deep tissues isolated the same organism, after standard and enriched culture.

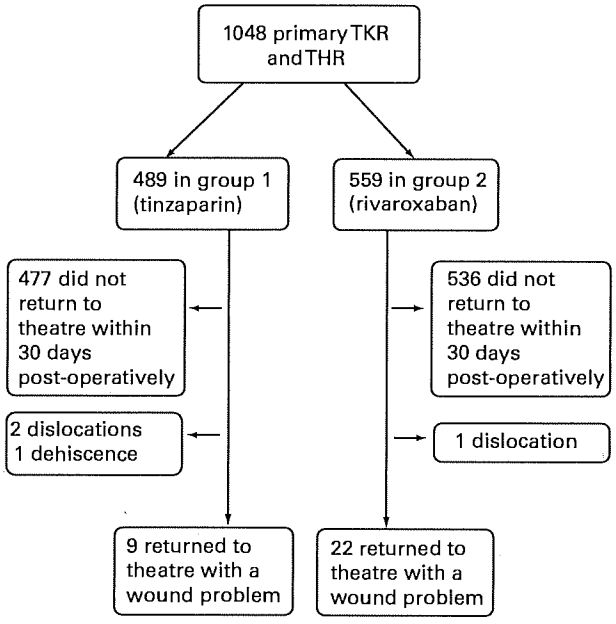

Fig. 1

Study design showing the consort flowchart (TKR, total knee replacement; THR, total hip replacement).

Statistical analysis. Analysis was on an intention-to-treat basis. All statistical analyses were performed using SPSS version 14.0 (SPSS Inc., Chicago, Illinois). Categorical data were analysed using a 2 × 2 contingency table with chi-squared and Fisher's exact tests as dictated by sample size. Continuous data were analysed using the Student's *t*-test. The null hypothesis was that there would be no difference in the return to theatre rates between group 1 and group 2. Statistical significance would be reached at a confidence interval (CI) of 95% ($p < 0.05$).

Results

There were a total of 1048 patients in the study: 489 in group 1 and 559 in group 2. There were a similar proportion of THRs and TKRs performed in each group: 195:294 and 249:310, respectively (chi-squared test, $p = 0.13$).

In group 1 (tinzaparin), nine of the 489 patients (1.8%, 95% CI 0.9 to 3.5) returned to theatre with wound complications. In group 2 (rivaroxaban), 22 of 559 patients returned to theatre (3.94%, 95% CI 2.6 to 5.9). This increase was statistically significant ($p = 0.046$). Demographics and comorbidities were similar in the subgroups of return to theatre patients (Table I).

Of those patients who returned to theatre, microbiology results showed that five of the nine (55.5%) in group 1 had a deep infection, compared with 14 of 22 (63.6%) in group 2 ($p = 0.7$). The overall rate of deep infection in group 1 was 1% (95% CI 0.4 to 2.4), compared with 2.5% (95% CI 1.5 to 4.2) in group 2 ($p = 0.102$).

Rates of venous thromboembolism remained similar in both groups. The incidence of symptomatic radiologically confirmed pulmonary embolism was 0.8% (95% CI 0.24 to 2.16) in group 1 and 0.9% (95% CI 0.32 to 2.14) in group 2 ($p = 1.00$).

Analysis of the return to theatre patients (Table II) revealed that there was no statistically significant difference in the mean time from primary operation to return to theatre between groups 1 and 2 (17.22 days (8 to 25) *vs* 16.81 days (6 to 30), $p = 0.89$). Wound haematoma was the stated indication for return to theatre in significantly more cases after rivaroxaban was introduced (0 *vs* 9, $p = 0.032$). The return to theatre patients were more likely to require more than one washout (3 *vs* 9, $p = 1.00$) and a total joint revision (1 *vs* 2, $p = 1.00$) after rivaroxaban was introduced, but neither observation was statistically significant. The analysis of this subgroup based on THRs and TKRs separately is shown in Table III.

The mean length of hospital stay for the primary operation in patients who subsequently returned to theatre in group 1 (tinzaparin) was 6.1 days (2 to 8), and in group 2 (rivaroxaban) was six days (2 to 10). There was no statistically significant difference in the mean total length of stay for those patients who returned to theatre in groups 1 and 2 (21.0 days (10 to 32) *vs* 18.8 days (7 to 79), 95% CI -9.22 to 13.58, $p = 0.70$).

Discussion

Controversy exists over the routine use of chemical thromboprophylaxis in lower-limb arthroplasty. In 2007, 2009 and 2010 NICE published guidelines recommending extended-duration chemical thromboprophylaxis for all patients undergoing lower-limb arthroplasty within the NHS in England and Wales.[14] Subsequent correlation of the National Joint Registry (England and Wales) and the Hospital Episode Statistics[15] data has shown an increased rate of venous thromboembolism in patients undergoing THR despite an increased use of low molecular weight heparin chemical thromboprophylaxis. Additional concern exists regarding an increase in the incidence of complications associated with chemical thromboprophylaxis, such as prolonged wound drainage[12] and thrombocytopenia.[15,16]

The RECORD trials were deficient in their lack of measurement of surgical outcomes such as wound healing, drainage, infection, range of movement and chronic pain. This led one of the authors of the RECORD4 paper[2] to later state that he would not recommend it (rivaroxaban) for his patients.[10]

Prolonged wound drainage after lower-limb arthroplasty is associated with infection, longer hospital stay, re-operation, and a subsequent increase in the economic burden on the national resources.[17] We could not find any reports focusing on the potential wound complications associated with the use of oral factor Xa inhibitors such as rivaroxaban.

In this study period, patients who received rivaroxaban were more than twice as likely to return to theatre with a wound complication after THR or TKR as those who received tinzaparin (3.94% *vs* 1.8%, $p = 0.046$). In both groups, patients having a THR were more likely to return to theatre compared with those having a TKR (group 1, 8 *vs* 1, $p = 0.004$, and group 2, 16 *vs* 6, chi-squared test, $p = 0.015$) (Table III).

Separating the TKR from the THR patients still shows an increase in the rate of return to theatre after changing from tinzaparin to rivaroxaban as the thromboprophylactic agent. In the TKR patients the rate increased from 0.3% (1 of 294) to 2% (6 of 249) after the change to rivaroxaban. This was statistically significant ($p = 0.05$). In the THR patients the rate increased from 4.1% (8 of 195) to 5.2% (16 of 310), but this did not reach statistical significance ($p = 0.67$) (Table III).

Post-operative wound infection remains a major burden on both the patient and the healthcare provider. Deep infection following arthroplasty is a high-morbidity complication that often requires many surgical debridements, protracted courses of expensive and potentially toxic antibiotics, prolonged hospital stay with immobilisation and isolation, and frequently staged revision procedures.[21] Our rate of infection increased from 1% to 2.5% following the introduction of rivaroxaban. An infection rate of 1% is similar to that reported in the literature following hip and knee replacement.[22,23]

Table II. Further analysis of return to theatre (RTT) patients: nine in the tinzaparin group (T1 to 9) and 22 in the rivaroxaban group (R1 to 22)

Patient	Primary operation*	RTT indication	Time to RTT (days)	Infection	Organism	> 1 RTT (washout)	Revision
T1	THR	Wound ooze	20	No		No	No
T2	THR	Wound ooze	8	No		No	No
T3	THR	Wound ooze	11	No		No	No
T4	THR	Wound ooze	15	Yes	*S. epidermidis* (resistant)	Yes	Yes
T5	THR	Wound ooze	25	Yes	*Staph. aureus*	Yes	No
T6	THR	Wound ooze	16	Yes	*Staph. aureus*	Yes	No
T7	TKR	Wound ooze	18	Yes	*Staph. aureus*	No	No
T8	THR	Wound ooze	22	Yes	Coagulase-negative staphylococcus	Patient refused	No
T9	THR	Wound infection	20	No		No	No
R1	TKR	Wound ooze	29	Yes	*Klebsiella sp.*	Yes	No
R2	THR	Wound ooze	11	Yes	*S. epidermidis*	Yes	No
R3	THR	Discharging haematoma	7	No		No	No
R4	TKR	Wound infection	30	No		No	No
R5	THR	Discharging haematoma	10	No		No	No
R6	TKR	Wound ooze	23	Yes	Coliforms	No	No
R7	THR	Discharging haematoma	13	Yes	*S. epidermidis*	No	No
R8	THR	Wound ooze	16	Yes	*S. epidermidis*	No	No
R9	THR	Wound ooze	23	No		Yes	No
R10	THR	Discharging haematoma	8	No		Yes	No
R11	THR	Wound ooze	14	No		No	No
R12	THR	Wound ooze	6	No		No	No
R13	TKR	Discharging haematoma	30	Yes	*E. coli*	Yes	No
R14	TKR	Discharging haematoma	14	Yes	*E. coli*	No	No
R15	THR	Wound ooze	26	Yes	*S. epidermidis*	Yes	No
R16	TKR	Discharging haematoma	21	Yes	MRSA†	Yes	No
R17	THR	Wound ooze	30	Yes	*Staph. aureus*	Yes	Yes
R18	THR	Discharging haematoma	10	Yes	*Staph. aureus*	No	No
R19	THR	Wound ooze	9	Yes	*S. epidermidis*	No	No
R20	THR	Wound ooze	14	Yes	*S. epidermidis*	Yes	Yes
R21	THR	Discharging haematoma	13	Yes	Coliforms	Yes	No
R22	THR	Wound ooze	13	No		No	No

* THR, total hip replacement; TKR, total knee replacement

† MRSA, methicillin-resistant *Staphylococcus aureus*

Table III. Analysis of the rates of infection and return to theatre by the type of arthroplasty

	Tinzaparin		Rivaroxaban	
	THR* (n = 195)	TKR† (n = 294)	THR (n = 310)	TKR (n = 249)
Return to theatre (%)	8 (*4.1*)	1 (*0.3*)	16 (*5.2*)	6 (*2.4*)
Infection (%)	4 (*2.1*)	1 (*0.3*)	9 (*2.9*)	5 (*2.0*)

* THR, total hip replacement

† TKR, total knee replacement

Our rate of venous thromboembolism events remained unchanged; however, the study size would be underpowered to detect a difference, and no meaningful statistical analysis could therefore be performed.

On further detailed analysis of the return to theatre cases it was noted that the stated indication for this was a 'wound haematoma' in significantly more cases after rivaroxaban was introduced (0 *vs* 9, p = 0.032).

The mean hospital length of stay for a primary TKR or THR in our hospital at the time of this study was 5.3 days (1 to 79). Patients who subsequently had wound complications and returned to theatre were noted to have a slightly longer mean length of stay. It may have been that this was because of concerns over their persistently leaking wounds, but data here are lacking. The mean total length of stay in these patients (including the initial stay for the primary procedure as well as the return to theatre hospital stay) was 22 days (7 to 79). There was no statistically significant difference in the mean total length of stay between groups 1 and 2 (p = 0.70); however, the observed increase in the number of return to theatre patients in the rivaroxaban group led to an overall increase in the total number of extra hospital days required for this group.

Several cost-effectiveness models have shown oral anticoagulants, including rivaroxaban, to be more effective and less expensive than enoxaparin sodium;[24,25] however, these models fail to take into account the risk of prolonged wound drainage, post-operative infection and haematoma, which are known to have high personal, healthcare and socioeconomic costs.

Our hospital was one of the first in the United Kingdom to introduce rivaroxaban as thromboprophylaxis for all THRs and TKRs. In the RECORD trials, enoxaparin was used as the control drug,[1-4] however, tinzaparin was used as the control drug in this trial, as this was the established Trust protocol. Direct comparison trials in THR have shown enoxaparin to be of equal efficacy and safety to tinzaparin.[26]

This was a retrospective, non-randomised cohort trial, and therefore cannot causally link the use of rivaroxaban with an increased rate of wound complication; however, the only variable that changed in the study period was the chemical prophylaxis.

The retrospective nature of the study may be considered as a potential weakness, but also a potential strength, as the surgeons' decision was not influenced by an ongoing prospective study. Other weaknesses include a disparate group size and multiple surgeons in the series. The study durations, and hence group sizes for groups 1 and 2 were unequal. Retrospective analysis could not be extended beyond February 2009, as antibiotic prophylaxis changed at this point in a drive to reduce iatrogenic *Clostridium difficile* colitis associated with cephalosporins. Operations in both groups were carried out by the same nine surgeons, including three authors (PFP, MRR, SDM).

Thromboembolism after arthroplasty is considered to be a potentially serious complication. The incidence of venous thromboembolism events in the practice of modern arthroplasty has been challenged;[27] however, current NICE guidelines continue to recommend extended chemical prophylaxis.

The risk of venous thromboembolism needs to be balanced against the potential medical and surgical complications of the drug used to prevent it. The RECORD trials do not adequately assess these surgical complications, and focus only on the risk of major bleeding. Our study demonstrates the urgent need for further randomised controlled clinical trials to assess the safety and efficacy of rivaroxaban in clinical practice, focusing on the surgical complications as well as the potential prevention of venous thromboembolism. Based on this study, we have discontinued the use of rivaroxaban in our hospital until robust evidence from independent randomised clinical trials becomes available.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References

1. **Kakkar AK, Brenner B, Dahl OE, et al; RECORD2 Investigators.** Extended duration rivaroxaban versus short-term enoxaparin for the prevention of venous thromboembolism after total hip arthroplasty: a double-blind, randomised controlled trial. *Lancet* 2008;372:31-9.
2. **Turpie AG, Lassen MR, Davidson BL, et al; RECORD4 Investigators.** Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty (RECORD4): a randomised trial. *Lancet* 2009;373:1673-80.
3. **Eriksson BI, Borris LC, Friedman RJ, et al; RECORD1 Study Group.** Rivaroxaban versus enoxaparin for thromboprophylaxis after hip arthroplasty. *N Engl J Med* 2008;358:2765-75.
4. **Lassen MR, Ageno W, Borris LC, et al; RECORD3 Investigators.** Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty. *N Engl J Med* 2008;358:2776-86.
5. **Atkins RM.** NICE and venous thromboembolism. *J Bone Joint Surg [Br]* 2010;92-B:609-10.
6. **Van Thiel D, Kalodiki E, Wahi R, et al.** Interpretation of benefit-risk of enoxaparin as comparator in the RECORD program: rivaroxaban oral tablets (10 milligrams) for use in prophylaxis in deep vein thrombosis and pulmonary embolism in patients undergoing hip or knee replacement surgery. *Clin Appl Thromb Hemost* 2009;15:389-94.
7. **Longo UG, Maffulli N, Denaro V.** Rivaroxaban versus enoxaparin after total knee arthroplasty. *Lancet* 2009;374:681-2.
8. **Raju NC, Dimmitt S, Eikelboom JW.** Rivaroxaban versus enoxaparin after total knee arthroplasty. *Lancet* 2009;374:681.
9. **Stief T.** Rivaroxaban versus enoxaparin after total knee arthroplasty. *Lancet* 2009;374:681.
10. **Gómez-Outes A, Suárez-Gea ML, Blázquez-Pérez A, Poxo-Hernández C, Vargas-Castrillón E.** Rivaroxaban versus enoxaparin after total knee arthroplasty. *Lancet* 2009;374:682.
11. **Lotke PA.** Rivaroxaban for thromboprophylaxis. *N Engl J Med* 2008;359:2174.
12. **Patel VP, Walsh M, Sehgal B, et al.** Factors associated with prolonged wound drainage after primary total hip and knee arthroplasty. *J Bone Joint Surg [Am]* 2007;89-A:33-8.
13. **Saleh K, Olson M, Resig S, et al.** Predictors of wound infection in hip and knee joint replacement: results from a 20 year surveillance program. *J Orthop Res* 2002;20:506-15.
14. **No authors listed.** Venous thromboembolism: reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in inpatients undergoing surgery. NICE clinical guideline 46, 2007. http://www.nice.org.uk (date last accessed 15 March 2010).
15. **Jameson SS, Bottle A, Malviya A, Muller SD, Reed MR.** The impact of national guidelines for the prophylaxis of venous thromboembolism on the complications of arthroplasty of the lower limb. *J Bone Joint Surg [Br]* 2010;92-B:123-9.
16. **Pitto RP, Hamer H, Heiss-Dunlop W, Kuehle J.** Mechanical prophylaxis of deep-vein thrombosis after total hip replacement: a randomised clinical trial. *J Bone Joint Surg [Br]* 2004;86-B:639-42.
17. **Maderazo EG, Judson S, Pasternak H.** Late infections of total joint prostheses: a review and recommendations for prevention. *Clin Orthop* 1988;229:131-42.
18. **Eriksson BI, Kakkar AK, Turpie AG, et al.** Oral rivaroxaban for the prevention of symptomatic venous thromboembolism after elective hip and knee replacement. *J Bone Joint Surg [Br]* 2009;91-B:636-44.
19. **Clayton RA, Gaston P, Howie CR.** Oral rivaroxaban for the prevention of symptomatic venous thromboembolism after elective hip and knee replacement. *J Bone Joint Surg [Br]* 2010;92-B:468.
20. **Treasure T, Chong LY, Sharpin C, et al.** Developing guidelines for venous thromboembolism for The National Institute for Clinical Excellence: involvement of the orthopaedic surgical panel. *J Bone Joint Surg [Br]* 2010;92-B:611-16.
21. **Bryne AM, Morris S, McCarthy T, Quinlan W, O'Byrne JM.** Outcome following deep wond contamination in cemented arthroplasty. *Int Orthop* 2006;31:27-31.
22. **Fender D, Harper WM, Gregg PJ.** Outcome of Charnley total hip replacement across a single health region in England: the results at five years from a regional hip register. *J Bone Joint Surg [Br]* 1999;81-B:577-81.
23. **Lehtimäki MY, Kautiainen H, Lehto UK, Hämäläinen MM.** Charnley low-friction arthroplasty in rheumatoid patients: a survival study up to 20 years. *J Arthroplasty* 1999;14:657-61.
24. **Wolowacz SE, Roskell NS, Maciver F, et al.** Economic evaluation of dabigatran etexilate for the prevention of venous thromboembolism after total knee and hip replacement surgery. *Clin Ther* 2009;31:194-212.
25. **McCullagh L, Tilson L, Walsh C, Barry M.** A cost-effectiveness model comparing rivaroxaban and dabigatran etexilate with enoxaparin sodium as thromboprophylaxis after total hip and total knee replacement in the Irish healthcare setting. *Pharmacoeconomics* 2009;27:829-46.
26. **Planès A, Samama MM, Lensing AW, et al.** Prevention of deep vein thrombosis after hip replacement: comparison between two low-molecular heparins, tinzaparin and enoxaparin. *Thromb Haemost* 1999;81:22-5.
27. **Cusick LA, Beverland DE.** The incidence of fatal pulmonary embolism after primary hip and knee replacement in a consecutive series of 4253 patients. *J Bone Joint Surg [Br]* 2009;91-B:645-8.

EXHIBIT DX13

TO DECLARATION OF BENJAMIN W. HULSE IN SUPPORT OF DEFENDANTS' MOTION FOR RECONSIDERATION OF THE COURT'S DECEMBER 13, 2017 ORDER ON GENERAL CAUSATION

UNITED STATES DISTRICT COURT
DISTRICT OF MINNESOTA

Louis Gareis and Lillian Gareis, Plaintiff,	VOLUME I
v.	File No. 16-CV-4187 (JNE/FLN)
3M Company and Arizant Healthcare, Inc., Defendant.	May 15, 2018 Minneapolis, Minnesota Courtroom 12W 9:03 a.m.

BEFORE THE HONORABLE JOAN N. ERICKSEN
UNITED STATES DISTRICT COURT JUDGE

(JURY TRIAL - VOLUME 1)

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Proceedings recorded by mechanical stenography; transcript produced by computer.

PROCEEDINGS

(9:03 a.m.)

(Jury in.)

THE COURT: Good morning, everybody. Go ahead and be seated. Members of the jury, you can sit now wherever you went. I was so firm yesterday about how you had to sit in a particular seat, and we no longer care. I understand that some judges make jurors sit in the same seat all through trial, but I think what if you want to change? Please be seated everybody. What if you want to change or what if you decide you can't hear or see or you get sick of your neighbor or anything like that. So from now on, you have that limited amount, you have that limited amount of freedom.

And as I told you yesterday, we're going to start with the opening statements of the lawyers. Remember that the opening statements have the purpose of previewing for you what the lawyers think the evidence is going to be. The statements themselves are not evidence. Let me just ask the lawyers if they're ready. Ms. Zimmerman, are you ready?

MS. ZIMMERMAN: Yes, Your Honor.

THE COURT: And over here, Mr. Blackwell?

MR. BLACKWELL: Yes, Your Honor.

THE COURT: And the plaintiff being the party with the burden goes first. Ms. Zimmerman, we are ready to hear

from you.

MS. ZIMMERMAN: Thank you, Your Honor.

OPENING STATEMENT BY MS. ZIMMERMAN

May it please the Court, counsel, Mr. And Mrs. Gareis's, and Ladies and Gentlemen of the Jury:

My name is Genevieve Zimmerman, and I'm one of the plaintiff's lawyers who gets to represent these fine folks. And as the Judge has instructed you, I get to provide you a little bit of a road map about what we expect the evidence is going to show during this trial.

A couple of signs that I would suggest will help guide your receipt of this evidence. Listen carefully for risk and utility. The risk of using the Bair Hugger in an orthopedic surgery. Listen to hear if you have presented to you any evidence about utility, benefit of using the Bair Hugger in orthopedic surgery.

So what is the Bair Hugger? You've been waiting all day yesterday and now today to hear a little bit more about it. The Bair Hugger is a patient warming device. There is actually one of them right here. This is the exact -- not the exact model that was used in Mr. Gareis's surgery. It's a Model 505. One like this was used in Mr. Gareis's surgery.

I'm going to turn it on. And hot air is blowing

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out of the hose. Now, this device is connected to a disposable blanket. It comes in a package like this. Forgive me if I'm a little nervous.

It feels a little bit like a bib that they put on if you go to the dentist to keep your clothes clean. So it's paper and plastic. And when you plug the machine, this end on the paper end of this, it will fill up with air, and one side has hundreds of little holes. You'll get a chance to look at this later, but it blows up. It looks a little bit like a pool floaty and it blows the warm air down onto a patient. And this is how it works. And it's intended to be used in an operating room.

So what do we know about the environment of use for this machine? Well, it's used in an operating room. This is just an operating table. Patients are placed on this to have a surgery. They're anesthesized. They're not breathing on their own sometimes. Their body is cut open. You'll hear testimony about that. And so the physicians and the nurses and the anesthesia team that take care of these patients, they do everything they can to keep the patient safe.

One of the things that you'll hear about during the course of this trial is that the HVAC system, the air that comes down from the ceiling, it operates a little bit like a force field. I'm getting ahead of myself already.

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So one of the things that you'll hear also is that in a surgery the entire surgery team, the surgeons, the nurses, they're all taught that anything below the level of the surgery table, below the level of the table, that's considered dirty. It's considered dirty air.

And what happens with that HVAC system, air comes in from the ceiling, and it creates a kind of force field. It pushes down any kind of particles that carry germs and bacteria to the floor, and then there are vents that take those germs or bacteria, particles out of the room. It's a kind of force field intended to protect the patient.

What is a Bair Hugger? It sits on the floor. You'll hear from the anesthesia team that provided care for Mr. Gareis that it was sitting either on the floor or a few inches above the floor right under the head of the patient by the anesthesiologist or the CRNA during the course of the surgery and that's where it's intended to be placed. And what happens is you can kind of hear the machine starts to heat up air. It blows air through that hose. It fills up the blanket. You can kind of see on this example that it looks a little bit like a pool floaty, and then what happens is the patient is draped on top of that.

So they put all kinds of drapes up, and you'll hear testimony about that. But because of the drapes, that hot air that continues to pour out of those little holes in

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the blanket starts to fill up the space underneath the drapes. And you'll hear testimony about that from both experts and researchers.

And at some point, some of that hot air escapes the bottom edge of the drape. And what happened when hot air escapes the bottom edge of the drape? It rises because heat rises. And what happens then? It interferes with the force field that's intended to protect the patient. That's what happens. That's what the evidence will show in this trial.

How do we know that? Well, in getting ready for this trial, we went out and we found the best experts in the world. They're from across the country even world renowned experts. You're not going to hear any kind of disputes about qualifications from the folks we brought in to see you.

And the first person I would like to introduce you to who you are going to hear from is Dr. Said Elgobashi. He is a professor in mechanical and aerospace engineering. He is at the University of California, Irvine. He is a world class engineer. A world class engineer. He will come in. He will explain to you how he studied the effect of the Bair Hugger on an operating room. He'll explain to you how he used the same methods, the same kind of principles of physics, the principles of thermodynamics. The same kind of

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math equations to study the impact of this machine on an operating room. And how did he do that?

Well, what he did is he took a model operating room. And he does something by the way called computational fluid dynamics. You may hear the word CFD. That's what it stands for. I've been practicing that one for a while. So what he does is he studies the movement of particles in what's called turbulent flow. Everybody here agrees, and the evidence will be consistent with this, everybody agrees that the airflow in the operating room is turbulent air.

And so what Dr. Elgobashi studies is what happens to particles when there is turbulent movement? And he did two kinds of simulations. The same exact simulations he does for the U.S. Navy, the National Institute of Health, for NASA, and he ran these simulations, these CFD models on the super computers. And what he did is he put 3 million little particles on the floor in this model OR, and he used these mathematical equations to calculate exactly where each one of these particles moves, tiny second by tiny second. So every time one little particle moves then it recalculates where everything else went.

So this took millions of hours of computer time. And I'll show you what his CFD showed with respect to the normal operating room. So the colors on the bottom red, yellow and green, they're just so that you can see where the

UNITED STATES DISTRICT COURT

DISTRICT OF MINNESOTA

Louis Gareis and Lillian Gareis, Plaintiff, v. 3M Company and Arizant Healthcare, Inc., Defendant.	)	VOLUME II File No. 16-CV-4187 (JNE/FLN) May 16, 2018 Minneapolis, Minnesota Courtroom 12W 9:11 a.m.

BEFORE THE HONORABLE JOAN N. ERICKSEN
UNITED STATES DISTRICT COURT JUDGE

(JURY TRIAL - VOLUME II)

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Proceedings recorded by mechanical stenography; transcript produced by computer.

PROCEEDINGS

(9:11 a.m.)

(In open court with the jury present)

THE COURT: Good morning. Please be seated everybody. Welcome back.

Please be seated. And, Ms. Conlin, we are in the middle of Dr. Presnal's middle or somewhere.

MS. CONLIN: Yep, we're going to recall to the stand by way of video deposition Dr. Presnal. Your Honor, we played part of it yesterday. We're picking up at page 27, line 1.

THE COURT: Thank you.

(Video deposition of Dr. Bradley Presnal played as follows)

Q. Now, unfortunately, Mr. Gareis developed an infection after this, correct?

A. Yes.

Q. Do you know what type of infection it was?

A. Let me see if I can find it here. So when I saw him in August of 2011, he came back in with some pain so he did a --

Q. What page are you on, sir? There should be a number down at the bottom there?

A. 25, 000. So I had actually seen him before that because he came back in said his hip was starting to bother him. That was July of 2011, and he came back in because his hip

had done well initially but then started having some pain and so we sent him in for some blood work, a CRP, C-reactive protein and a sedimentation rate.

Q. What does that tell you?

A. So those are inflammatory markers, generally if they're elevated, if both are elevated that can be a sign of infection so that's when we use two because one alone may not be very indicative of an infection. I was trying to see if we had those results. I have in my note both the CRP and sed rate were elevated which can be an indication of infection, and so we did an aspiration. We drew fluid off his hip to check for infection. It came back with a coag-negative staph.

Q. What kind of organism is that?

A. So it's kind of a slow growing organism. It typically doesn't make people very ill. You know, high fevers, night sweats, things like that. Generally, just creates pain at some point. It's a hard one to diagnose sometimes because it's hard to grow in the lab. Sometimes you can get, you know, inconsistent cultures with it. And sometimes the only thing it causes is pain. People don't have any other symptom you would expect with an infection.

Q. Was his symptomology consistent with that type of infection?

A. I think so where he comes in, he's not feeling bad, just

A. **Well, that's an area of debate, but decades of -- research dating back decades have even said as many as one bacteria. But it's just probably several.**
Q. Okay.
A. **Just a few.**
Q. Just a few?
A. **Just a few. But very respective researchers have said one.**
Q. You used the term "ultra-clean." Can you define what that means.
A. **When you package an implant, it is truly sterile. It's packaged in a factory in a clean room where there's no bacteria, and that's sterile. That's the true definition of sterility, where there's no viable organism. A bacteria is an organism. And when you take that component out of the package to put it into the patient, it's now in the air.**
Unfortunately, even though this looks clean in here, the room and air looks clean -- you can't see clouds or smoke -- there is all this microscopic stuff going on in the air right now. And it will then no longer then be 100 percent sterile. It's going to be ultra-clean. That is it might have bacteria on it. It might not have bacteria on. Any time there is a chance it might have bacteria on it, then it's what we call ultra-clean.
We try to make the -- we try to make the room as

sterile as we can, but we never can get to a one hundred percent sterility. The good news is we know that if we keep that level of bacteria down to a certain amount, then the chance of you not having infections is really low.
THE COURT: Meaning you have an infection?
THE WITNESS: Chance of you having an infection, yes, Your Honor. It's really low if you can keep that down. So you have to control the environment and make it an ultra-clean environment.
It's one of the reason why when I open these components, I only open them the minute I need them. So I believe I'm actually putting a sterile component in because I'm not letting the environment see this component for very long. So that's one way I control the environment, is just open it when I need it. Everybody on my team knows that, and that's standard of care.
BY MR. FARRAR:
Q. Are there, those components, are they -- tell me how they are packaged.
A. **They're packaged many different ways, but they are often three layers. So there is a package within a package within a package. And the exact mechanics of how the factory does it, I'm not an expert in that, but it's done in a clean room basically where it's free of bacteria and organisms.**
Q. If there are bacteria organisms above the open incision,

can they attach to the prosthesis?
A. **Surely. One thing to think about is every room has bacteria, skin cells. Humans shed up to 10 to the 9th. I think that's about 100 billion skin cells a day. So it's an amazing number that humans shed of their skin.**
Skin cells also have bacteria. There's also particles that have bacteria on them. And there is lint and dust that have bacteria on it. This is all floating in the air right in here. It's kind of gross to think about. But there's plenty of studies that date back many decades and even recently -- one I saw in 2012, a study that showed that the floors are full of skin, and dust, and bacteria. What happens is it's in the air and then it settles on the floor. And that happens when people walk into a room.
So I imagine this room is cleaned every day, and most rooms in public-use buildings are cleaned every day. And if we were to study this room before all of us came in here, we would find a whole lot less microbiological load in here, meaning a lot less skin cells, a lot less bacteria, a lot less dust, particles. A lot of its on the floor. Some of it's floating in the air -- a lot of it's floating in the air. But when we all came in here -- no offense taken, Your Honor, including Your Honor --
THE COURT: Leave me out of this.
THE WITNESS: Okay, I will. And me, the officers

of the court, y'all, the spectators, we just brought in trillions of stuff into this room. It's really gross to think about, but that's what we did. And all of that has potential bacteria.
You can't make an operating room a clean room. Maybe one day in the future, space, in 2200 or 2300 or something like that we might have a clean room we can operate in, and that will be a happy day. Right now we can't do that.
So as soon as all of us walk into the room and we bring in all of our stuff, we have to have a way to protect the patient. That's what ultra-clean is all about, is trying to protect the patient from having all the stuff -- bacteria, skin cells, particles, lint, dust -- that just is naturally on you and falls off you get into the wound. The way we do that is through a lot of different mechanisms. I don't know if you want me to go into it.
BY MR. FARRAR:
Q. No, I do. I want to talk about what you as an orthopedic surgeon -- what orthopedic surgeons in general do to protect the patients from surgeries. I want to start with the ventilation system if we would.
If you could put up 1606.
So, Doctor, I'm showing -- this is, obviously, not to model Mr. Gareis' operating room, sort of a generic

operating room, but I want to talk about the ventilation. Describe to me what unidirectional flow is and how it protects the patient from infection risks.

A. **This is what I'm talking about. When we walk into a room, we bring a bunch of our stuff with us. What I tell my team every day and they say, Yeah, Doc, we know, bacteria is your number one enemy. Well, it is. It's my number one enemy because it's my patient's number one enemy.**

The way we do it is create a unidirectional -- protect the patient is create a force field is that you can see -- can I draw on this?

Q. Yep.

A. **This is -- up here are the diffusion panels where air is being -- clean air is being pushed through into the operating room. And it pushes those falling skin cells, and lint, and dust, and everything that we don't like on our patients down and out, so away. It's basically creating this force field that the patient is in, and all that stuff is being exhausted to the returns or the exhaust fans in the room.**

So clean air coming down. How we get that clean air? We do it through filtered air. We have a filter that is often a HEPA filter and close to one hundred percent filtration -- never one hundred percent because we're humans; I think it's 99.97 percent filtering out at a

certain size of particle. And not just that filter, that filter will be right here before the diffusion panels, but there's another one downstream from it and then another one often downstream from that. Sometimes an ultraviolet light is thrown into the mix where it's also killing bacteria. So you have filter, ultraviolet light, filter, filter, air coming into the operating room. We're doing the best humanly possible. It's not the best we will have one day, but it's the best right now.

Q. The ultraviolet light, does it eradicate particles or bacteria?

A. **The ultraviolet light will kill bacteria on particles.**

Q. So the bacteria are riding on the particles?

A. **That's right.**

Q. I'm sorry, I didn't mean to interrupt you.

A. **So it's pushed down, and then that's called unidirectional flow. And then it's pushed out the exhaust fans.**

And I think it's very important, that dates back to Sir John Charnley. He was knighted for his work in orthopedic surgery. He's an amazing man. He's a man that most orthopedic surgeons revere because he came up with this (indicating). He invented it. But he also began the work, early work, on unidirectional airflow and protecting patients. And subsequent studies over the last several

decades have shown it to be very important in protecting the patient.

MR. FARRAR: Your Honor, can I pull over the board and draw on it?

THE COURT: Well, sure. Go ahead.

MR. FARRAR: We'll do it at the lunch break.

THE COURT: It's finding a location that doesn't block everybody's view that's a challenge.

MR. FARRAR: We'll do it at break and we'll figure it out. It will be easier.

BY MR. FARRAR:

Q. You talked about force field -- sort of a force field. I think that's also known as a sterile field. Is that right?

A. **Yes, sir.**

Q. That's kind of the professional term for it?

A. **Yes, sir.**

Q. All right. Tell me where the sterile field, if you can draw on this -- I'll clear out what you've got -- tell me where the sterile field is.

A. **Okay. So this is the operating room table (indicating). That's ground zero. That's where the patient is. And I like to say it's all about the patient, nothing else. Everything we do is about the patient. So we want to protect the patient. That's ground zero, the sterile field.**

Anything below this is not sterile, is not ultra-clean.

And often you'll have tables that are used in the operating room, and those are in the sterile field as well. This table is out of the sterile field, but you can think of that gray zone as the sterile field. If this table were in here, there would be a surgery tech standing next to it, and it would be covered with sterile drapes that they go to school to learn how to do. That's the biggest part of their training, is learning how to sterilely drape tables and sterilely drape patients. They spend a lot of time going over that. They're very good at it. Very proud of the surgery techs I work with. They do a fantastic job protecting our patients.

Q. I put up another slide that shows the red below the operating room table. Would you consider that area sterile or is it not sterile?

A. **I think that's a pretty good pictorial of what's not sterile. Basically, the reason why surgeons have their hands up you see in TV -- they don't necessarily have them up like this, but --**

Q. That's for the shows, right?

A. **Yeah. But he can be down here about waist level. Anything between waist or table level is not sterile. It's where it's a danger zone.**

Q. Are surgeons careful not to have anything that's below

UNITED STATES DISTRICT COURT
DISTRICT OF MINNESOTA

Louis Gareis and Lillian Gareis, Plaintiff, v. 3M Company and Arizant Healthcare, Inc., Defendant.

VOLUME III
File No. 16-CV-4187 (JNE/FLN)
May 17, 2018
Minneapolis, Minnesota
Courtroom 12W
12:20 p.m.

BEFORE THE HONORABLE JOAN N. ERICKSEN
UNITED STATES DISTRICT COURT JUDGE

(JURY TRIAL - VOLUME III)

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Proceedings recorded by mechanical stenography; transcript produced by computer.

P R O C E E D I N G S

(12:17 p.m.)

(In open court with jury.)

THE COURT: Welcome back, everybody. Please be seated. And we'll have Dr. Stonnington back on the witness stand. You're still under oath from yesterday.

THE WITNESS: Yes, Your Honor.

THE COURT: And, Mr. Farrar, whenever you're ready.

REDIRECT EXAMINATION

BY MR. FARRAR:

Q. Doctor, welcome back. I have a few questions just followups. We're going to be pretty short. I want to talk to you about some of the other equipment that Ms. Pruitt talked to you about yesterday that's in the operating room. And if we're going to pull up the operating room, if you would do that, 1606. This is just a kind of a mock -- demonstrative.

But she talked about an anesthesia machine. If you just kind of point to where an anesthesia machine would be located.

A. It would be at either end of the table depending on what's the head or the -- you can use the table, the table has either got a head and a foot side, but you can actually switch them around. We sometimes do for certain different

types of operations, so anesthesia can be received from either side.

Q. Does the anesthesia machine blow air from the unsterile field on the patient?

A. No, it doesn't. In fact, the back of the anesthesia machine is where the air comes out of, and it's typically in every OR I've been in it's aimed away from the sterile field and that it's going towards the returns the exhaust fans where the air goes out.

Q. She asked you about electrocautery machine, is that also called a Bovie?

A. Yes, sir.

Q. What is a Bovie and where is it?

A. A bovie is basically a hot knife. And it's --

THE COURT: How do you spell Bovie? Like a Bovie knife?

THE WITNESS: It's b-o-v-i-e.

THE COURT: Oh, Bovie, not a boning.

A. Yeah, it's not a bowie knife or however you want to say it. It's not a Texas knife, I guess. It's a various thin pointed device that it heats up, and you can basically cut tissues and cauterize bleeding while you're going down, but you don't use it the whole way down either. I use a combination. I use a lot of dissection with my fingers.

Q. When you say "dissection," what do you mean?

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Q. The nurse anesthetist took a break, is that unusual in your practice?
A. That's very common. That's usual. In fact, it's a running joke among surgeons that we make fun of them anesthesia folks because they always have to have a lunch break, and they always have to have bathroom breaks and that's what they do. And, you know, they're working all day. At least after I get done with a case, I can go sit down in the lounge, but they actually, they got to keep getting patients back, so they rightfully deserve to have the breaks, but we make fun of them for that.

But that's what they do. So when they need to go to the bathroom, they get relieved. When they need to go to the lunch, they get relieved, and that's standard care across America.
Q. Is there anything unusual about it?
A. There's nothing unusual about it.
Q. There was questions regarding a rep from the manufacturer of the prosthesis in the room?
A. Correct.
Q. Do you typically have reps in the room when you're doing hip replacement surgery?
A. For joint replacements every case.
Q. Why?
A. The representative knows all the vital points about the

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prosthesis, so when you're putting this in, they know where the boxes are that contain the components that are a few millimeters different. They can answer questions about factory specifications that may or may not be right on the -- might not be available to the surgeon right there other than through the representative. They make sure that the prosthesis is the correct box is being chosen to open for the surgery.

They, in my practice, they will come into my clinic, and they will look at the x-rays of the patients I'm about to operate. They'll make measurements and go over the case, and we'll come up with a plan for the next day. They're actually a really vital part of the joint replacement care, and so that is typical for them to be in the room.
Q. Would you consider it part of the standard of care?
A. It is definitely part of the standard of care.
Q. So the number of folks in Mr. Gareis's surgery, is that consistent with the number of people that are in and out of the surgeries that you do?
A. That is, yes, that's typical. And we're not at a point in medicine where we're sitting, going to have, you know, maybe one day, you know, maybe we'll be this space ship society where we're going to have surgeons sitting in control rooms with joy sticks. We're going to have robots,

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everything is sterile, and no human is going in and out. But right now the best we have is what you just described, and we have to work with that. And so that's why we create an OR to diminish the effects of that. And just because it's like that, it's not a license to make it worse.
Q. When you say you create an OR to combat the effects, what are you talking about?
A. Going back to Sir John Charnley, who was united over his work on this, creating unidirectional airflow that protects the patient via this force field of getting the particles, the skin cells that are floating, the dust that is floating getting away from the patient and out to the return vents. And that's one of the reasons, that's the main reason we have that because we have to have human activity in the operating room. I have to be able to move my arms to do a surgery. I have to have a scrub nurse who can go from table to handing me an instrument. I have to have a circulator who can go get things that are necessary. It's -- the anesthesiologists have to take breaks. Those are all the things that are standard of care, but it's not a license to make things worse.
Q. You were asked a question about whether the patient's skin is a major source of bacteria. And you wanted to give an explanation, and you didn't get a chance to, but you do now, so I want to let you explain what you wanted to say

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about that to the jury, please.
A. So the skin is a major source of bacteria. And as far as it being a significant source, it's a significant source from the standpoint that there's not just the skin cells on your skin. We deal with the skin cells on your skin with the prep. It's the skin cells like I talked about in this room. It's the skin cells in the air, it's the skin cells on the floor. Those are in addition to the skin cells that are on your skin. It's what makes it significant is we have to figure out how to control the skin cells that are not controllable. And those are the -- and the best we can do to make them controllable is through unidirectional air. We control the skin cells on the skin through our prep and we try our best to control the skin cells through this unidirectional air through this force field which takes those cells, those particulates, that dust and pushes it out through the return vents and protects the patient, and so that's what I meant. Those skin cells carry bacteria. A significant percentage of them carry bacteria.
Q. The prosthesis, can you hold that up? How does a bacteria get from wherever it is on a skin cell onto that prosthesis during a surgery?
A. If you didn't have that force field protection from the unidirectional air, the skin cells can actually come up from the floor in the air and do that (witness indicates.)

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Q. Is that called airborne contamination?
A. That's airborne contamination, and that is through decades of research, that is the source of intraoperative infections.
Q. Can bacteria, do they have -- this is maybe a silly question, but do they have legs? Can they walk or jump?
A. They have to have a vector, and the vector is something that carries it to them. And it's the air, it's the air carrying it to them. So you have to have a way to control the air, to control those skin cells from getting on to the prosthesis and that's what we do. We control it through the unidirectional air.
Q. So if you're putting in a prosthesis like that into someone like Mr. Gareis, is it possible for bacteria that's on his skin while you're putting it in to jump on to the prosthesis?
A. Jump on it by itself?
Q. Right.
A. No, it's not. It needs something to bring it there. And what's interesting is when you prep a patient's skin, the Darouiche study from 2010 the New England Journal of Medicine, a significant study, it showed that when you prep a patient's skin with the best we have, which right now is in my opinion ChloraPrep, which I use, that showed a decrease infection rate at the skin level. It didn't show a

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decrease infection rate at the deep joint. So it shows that it's the air infecting the deep joint. It's not the skin because if it had been the skin, that study would have shown an increased infection rate of deep joints, and it didn't.
Q. So airborne contamination is what infects people for deep joint infections?
A. Airborne contamination dating back decades, decades of research.
MR. FARRAR: Your Honor, may I approach?
THE COURT: You may.
BY MR. FARRAR:
Q. The international consensus we talked about yesterday from both I asked you some questions and Ms. Pruitt asked you some questions about it, and this is the group of four hundred or so that get together every couple of years and discuss the best practices to prevent deep joint infections, correct?
A. Yes, sir.
Q. And I think I asked you this, but you find it authoritative and relied on it for opinions in this case, right?
A. I did.
MR. FARRAR: I'm going to ask questions on this, do you have any objection?
MS. PRUITT: No. It's not that I don't want to.

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BY MR. FARRAR:
Q. I want to, it's sort of a thick book, but I'm going to turn your attention if you would on the bottom to page 115.
A. I think I found it this time.
MS. PRUITT: Which number is that?
MR. FARRAR: It's question 2 on page 115.
MS. PRUITT: Where is the page?
THE WITNESS: Oh, I see it.
BY MR. FARRAR:
Q. Do you see where I'm looking, do you see question 2?
A. I do.
Q. All right. What's question 2 say?
A. "Do numbers of bacteria in the operating room environment correlate directly with the probability of SSI? Surgical site infection.
Q. And can you read what the consensus --
REPORTER: I'm sorry.
A. SSI means surgery site infection.
Q. And if you would read what the consensus is?
A. "We recognize that airborne particulate bacteria are a major source of contamination in the OR environment and that bacteria shed by personnel are the predominant source of these particles. The focus of our" -- do you want me to keep going?
Q. No, I really want to ask you about the justification and

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it says, "air is a potential source of contamination in the OR," and this is the part that I wanted to focus on.
A. Okay.
Q. "Studies have demonstrated that the number of airborne bacteria around the wound is correlated to the incident of periprosthetic joint infection." Can you tell the ladies and gentlemen of the jury what that means?
A. So it's the airborne bacteria that is correlated with the infection in the joint. It's airborne bacteria that is affecting the deep joint. It's not the skin. It's not the skin on the patient's skin. It's the airborne bacteria that are floating on skin or particles or dust that are then making their way into the wound and infecting that joint.
Q. I want to shift gears. You were asked some questions about Mr. Gareis having a prior total hip replacement on his other hip, and he had two other in his revision surgeries. And the questions were something about him using the Bair Hugger and not getting the infections in those, and I want to ask you is that significant to you as an orthopedic surgeon that he used the Bair Hugger in other instances and did not get an infection?
A. It is. To answer your question, that's not significant to me.
Q. Why not?
A. Because like I said, the operating room is not a robotic

UNITED STATES DISTRICT COURT
DISTRICT OF MINNESOTA

Louis Gareis and Lillian Gareis, Plaintiff, v. 3M Company and Arizant Healthcare, Inc., Defendant.	VOLUME IV File No. 16-CV-4187 (JNE/FLN) May 18, 2018 Minneapolis, Minnesota Courtroom 12W 9:04 a.m.

BEFORE THE HONORABLE JOAN N. ERICKSEN
UNITED STATES DISTRICT COURT JUDGE

(JURY TRIAL - VOLUME IV)

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PROCEEDINGS

(9:04 a.m.)

THE COURT: Dr. Jarvis, come on up.

Good morning, everybody. Please be seated. You're still under oath from yesterday. You can go ahead and take the seat.

And, Ms. Conlin, whenever you're ready.

MS. CONLIN: Yes, thank you, Your Honor.

DIRECT EXAMINATION

BY MS. CONLIN:

Q. Good morning, Dr. Jarvis.

A. Good morning.

Q. I want to just finish up on a couple points that we we're dealing with yesterday. I'd like to talk to you a little bit more about the studies that have been cited in this case.

I'd like to add a column for orthopedic procedures, and so could I direct your attention to the Zinc article first. Do you know how many of those were orthopedic procedures?

A. Zero.

Q. And how about in the Huang study?

A. Zero.

Q. How about Moretti?

A. 20.

Q. And how about Hall?

A. Zero.

Q. And in the interest of completeness, I'd like to add one other study, the Oguz study, if you could look in your book, sir, at Trial Exhibit 635. And is this article entitled, "Airborne Bacterial Contamination during orthopedic surgery a randomized control trial?

A. Correct.

Q. What did they find in that trial with respect to whether there was an increase in bacteria at the surgical site when the Bair Hugger was used?

A. Well, they did agar plates around the operating room, and the one that was closest to the patient, wasn't really real close, but the closest is table or plate 4 in the study and that had an increase that almost reached statistical significance.

Q. And how many patients were in the Oguz study?

A. There were a total of 80 patients that were randomized to the forced air warming Bair Hugger versus an electric blanket, and then they were divided into laminar flow and non-laminar flow, but the bottom line is of these were all minor orthopedic procedures so not implant procedures and there was only one total knee.

Q. How many patients total?

A. In the forced air warming, 40.

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for whether bacteria -- the presence of bacteria was assessed, and what the study says about causation.

The first one we'll start with is Legg. We'll call that Legg 1. Okay? This is one of the particle studies you relied on, right?

A. Correct.

Q. Let's start with number of patients. How many patients were involved in this study?

A. I guess it depends on if you take the volunteer as being a patient.

Q. We'll call them a patient. So that would be one, right?

A. Correct.

Q. Looked at three different particle sizes, right?

A. 0.3, 0.5, and 5 microns.

Q. 0.3, 0.5, and 5. We'll agree those are microns.

The increase in number of 0.3 micron particles from the Bair Hugger over no Bair Hugger, using that as a control, that would be 764, right? If you take the --

A. I need a calculator, but it looks like around that.

Q. Okay. And for the 0.5 size it would be Bair Hugger increased the number by 24. And for the 5 micron size increased it by 2.8?

A. Right. That's the mean number.

Q. Right, the mean number.

Now, these were just --

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A. None of those were statistically significant.

Q. Right. This was just looking at the ambient background, whatever particles happened to be in that otherwise empty surgical suite, right?

A. Well, it's not empty. It's got the volunteer, it has the forced air, the radiant heater in there, operating room table.

Q. Okay. But no surgical personnel coming in or out? There's no machinery operating? There's no actual surgery going on, right?

A. Correct.

Q. Okay.

A. Well, actually, there is a surgeon. So it is an assimilated operation.

Q. Okay. Did the surgeon use any equipment? Did he use the --

A. Wore sterile clothing, a theater hood, and body exhaust hose.

Q. No reason to think that he was actually using a saw or a drill or a reamer or electrocautery knife, you know, the suction?

A. Correct.

Q. Just two or three bodies in there, right?

A. Correct.

Q. Okay. Now, in the study itself does it say -- it

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doesn't say whether they attempted to culture bacteria or not, right?

A. That was not a part of their study.

Q. Okay. But you know that, in fact, they did try to culture bacteria? They couldn't find any?

A. And where does it say that?

Q. It doesn't say that, not in this paper.

A. Okay. You learned it somewhere else?

Q. You have read Dr. Legg's deposition testimony, haven't you?

A. Long ago.

Q. Okay.

A. But certainly in the paper about their methods, their abstract, their methods say the two things they were going to do was look at the impact on temperature and look at the impact on particle.

Q. Okay. Just to fill in my column I'm going to say -- you say not tested.

A. Well, not reported. Not tested.

Q. Or not reported. But I want to put an asterisk there. I'm going to ask the jury to see when they've heard all the testimony, if my memory is correct, that Dr. Legg did in fact try to culture bacteria but didn't get any.

MS. CONLIN: I'm going to object to him testifying.

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THE COURT: Sustained.

BY MR. COREY GORDON:

Q. If we would now move to the discussion portion on page P-0940003. Okay? Under Discussion, second paragraph, it says, Because of the nature of our experiment, we are unable to conclude that the use of the forced air warming device, which produced a change in temperature and an increase in the number of particles over the surgical site, would actually lead to an increased risk of surgical site infection. And one of the reasons they explain for why they are unable to do that is they -- in the next paragraph they say that the bacteria require particles to transport them, and although we are unable to confirm if any of the particles are transporting bacteria, the significant increase in the number of particles that we found at the surgical site is of concern.

So they were unable to confirm if any of the particles are transporting bacteria, but they were unable to conclude that the use of a forced air warming device, the Bair Hugger, would actually lead to an increased risk of surgical site infection, right?

A. Right, because they focused on the significant increase in temperature and the number of particles. Right.

Q. Right. But in my causation column you'll agree with me that they say no, this study does not show causation?

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A. Right. I guess I would say they didn't even look at it, so --
Q. Okay. And the second one that I think you rely on, we'll call it Legg 2. That's the Legg paper from 2013 -- excuse me, 20 -- yeah, it was published in 2013, P-96.
A. Oh, P-96. Which one is that? I have P-94 and then D, like dog, 96.
Q. There is a D-96 in the book, but the very next one is P-96.
A. Got it.
Q. I'm guessing under the Patients column you want to put 1, right?
A. Excuse me?
Q. Under the Patients column 1 because this was a -- or was there?
A. Correct.
Q. Well, they say it was a mannequin.
A. There is a surgeon, too.
Q. But I'm just counting patients the way you were counting patients.
A. Oh, okay.
Q. I'll do whatever you want. If you want to count a mannequin as a patient, I'll do it.
A. It's up to you. I don't care.
Q. You tell me. I'll give you the mannequin.

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Okay. What was the particle size?
A. What was that?
Q. What was the particle size? Let me speed this up. Look at the bottom of the first column on page 0002 where it says it can measure --
A. Greater than 0.3 microns.
Q. How were the particles generated? This wasn't just ambient particles, right? Top of that column. I directed you to the wrong place. Measuring device was at the bottom. But what the particles were is at the top of that column.
A. They were created by a Rocket PS 23 smoke machine.
Q. So it was a smoke generator, a fog?
A. Correct.
Q. And it was blowing out particles of what size?
A. 0.3 microns.
Q. Okay. And blowing out these particles from this machine there was an increase of -- it was huge, a couple million over -- yeah, over 2 million over control, right?
A. It used a what?
Q. There was a huge increase over the control using this smoke generator. With a Bair Hugger on versus Bair Hugger off there were more than 2 million more particles, right?
A. Correct.
Q. This says nothing about bacteria, right?
A. They did not look.

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Q. Okay. And on this one under Causation it says -- if you turn to the last page, page 0004 -- This study does not show that forced air warming increases the risk of infection, only that in certain types of theater set-up it can significantly disrupt the unidirectional airflow and draw particles from the potentially contaminated area below the sterile field -- sterile surgical field. So on causation that's a no, right?
A. And they say this is a concern.
Q. Right. But they don't conclude that there's any causation?
A. Well, they didn't look at SSIs. Yes.
Q. Okay. For Sessler, that's P-75. And this is the study in the Netherlands, right?
A. Correct.
Q. And the purpose of this test wasn't to measure absolute numbers of particles, right?
A. Well, it was looking at particle reduction, the DIN standard.
Q. I think you used the term "relative" impact on the unidirectional airflow. Right?
A. Correct.
Q. And without the unidirectional airflow on, it started out with 35 million particles, however they were measuring it. When they turned the laminar airflow system on, that 35

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million went down to under 1,000 when the Bair Hugger upper body blanket was used, the one that was used in Mr. Gareis' surgery, right?
A. Repeat that, please.
Q. Why don't you look at figure 2.
A. I am.
Q. Okay. And that's a logarithmic scale, right?
A. Looks like it.
Q. Which means that each space between the lines on the bar graph is a factor of 10. So from 1 to 10 is the first jump, but then the next jump isn't from 10 to 20, it's 10 to 100. The next jump is from 100 to 1,000, the next from 1,000 to 10,000, next from 10,000 to 100,000, 100,000 to a million, a million to 10 million, and so on.
The baseline, the total number of particles, however they were measuring it, started out somewhere between 10 million and 100 million?
A. Correct.
Q. Kind of crude, but say it's about 30, 35 million?
A. Yeah. I'd have to say I don't know in the paper if they ever give that exact number.
Q. I don't believe they do. That's why I'm --
A. It's a guesstimate.
Q. Okay. So big number, 35 million.
With the system on it goes down to somewhere

UNITED STATES DISTRICT COURT
DISTRICT OF MINNESOTA

Louis Gareis and Lillian Gareis, Plaintiff,	)	VOLUME V
v.	)	File No. 16-CV-4187 (JNE/FLN)
3M Company and Arizant Healthcare, Inc., Defendant.	)	May 21, 2018 Minneapolis, Minnesota Courtroom 12W 9:37 a.m.

BEFORE THE HONORABLE JOAN N. ERICKSEN
UNITED STATES DISTRICT COURT JUDGE

(JURY TRIAL - VOLUME V)

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PROCEEDINGS

9:37 a.m.

THE COURT: Good morning, everybody. Welcome back and please be seated.

Ms. Zimmerman. You may proceed.

MS. ZIMMERMAN: Thank you, Your Honor.

May it please the Court, for our first witness today the plaintiff's will call Dr. Said Elghobashi.

WITNESS DR. SAID ELGHOBASHI SWORN

THE COURT: Please take the witness stand, and once you're comfortable, state your full name, spelling your last for the record.

THE WITNESS: Said Elghobashi.

THE COURT: And spell your last name for the record.

THE WITNESS: E like echo, l-g-h-o-b-a-s-h-i.

DIRECT EXAMINATION

BY MS. ZIMMERMAN:

Q. Good morning, Dr. Elghobashi.

A. Good morning.

Q. Could you take a moment to introduce yourself for the ladies and gentlemen of the jury today?

A. My name is Said Elghobashi. And I'm a distinguished professor at the University of California.

Q. Thank you.

A. In mechanical and aerospace engineering.

Q. All right. Dr. Elghobashi both and you I sometimes are going to need to work on speaking into the microphone so the court reporter can take down everything we're saying, okay?

A. Sure.

Q. I know you have a quiet voice sometimes.

Dr. Elghobashi, what is your current employment?

A. University of California at Irvine.

Q. And I'm going to direct you there's a binder of materials in front of you. Can you turn to Tab 704?

A. I have to put my glasses on.

Q. That's fine.

A. Which number, please?

Q. 704. Towards the front.

A. I have it.

Q. Do you see that? And what do you see at Tab 704? What is that document?

A. My CV.

Q. All right. And is a CV a fancy way of saying your professional resume?

A. Yes.

Q. What is your educational background?

A. I have a master's degree in 1971 from U.S.C. That's the University of Southern California. I have a Ph.D. from University of London Imperial College in 1974. And I have a

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Science. These are the top scientists in physics, chemistry, biology, but not engineering. So when I was elected to the National Academy of Engineering, I was asked by the University to give a lecture to these distinguished professors at our school who do not know about the subject; so, therefore, I had to present it in a way that a person who never studied turbulence could understand. So I hope this will be also easy for you.

Q. All right. And, Doctor, the ladies and gentlemen of the jury have heard some mention of the word laminar referring to airflow that comes down from the ceiling?

A. Yes.

Q. What does this slide show?

A. It shows a faucet in a kitchen and very small flow rate coming, and you can see liquid water, and it looks like a lens. It's very clear. There's a white and yellow wall behind that. And you can see the water is so clear that you can see the white and yellow. That's a laminar flow. And laminar, the word "laminar" comes from Latin means composed of many laminae.

By the way, in any hospital room, in any hospital room people misuse the word laminar. There is no laminar flow in any operating room. Never. If you want to change the air in an operating room 25 times per hour, the flow is turbulent, period. But this one to show you the laminar,

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the turbulent, if you increase the flow rate in the faucet, you will see now the flow is vibrating, blurring, and you cannot see the distinction between the white and the yellow wall behind the water. So that's a turbulent flow. The same device, the only difference is increasing the flow rate.

Q. So have you ever used a garden hose?

A. Yes, a garden hose you can look at the flow coming out of the hose could be laminar or turbulent, depending on how much you turn the faucet on.

Q. All right. Or if you maybe put your thumb over the edge of the hose?

A. If you put your thumb, it depends on the flow rate. Again, it can be stalled on the steady laminar, or if it is gushing at high speed, it would be a turbulent flow.

Q. All right. And in any event, the airflow in an operating room is turbulent; is that right?

A. Always, always, but the many publication that says laminar flow, there is no laminar flow in the room, yeah. The flow in this room also is turbulent.

Q. All right. And the flow in this room for those of us that aren't engineers, what is flowing?

A. Okay. If you look at the faucet on the left or the right, the fluid coming, we call this fluid flow. It means if you switch the valve off, there would be no flow. Flow

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means a massive fluid, it could be liquid, water or gas or air moving from one place to place with a certain velocity. That's a flow.

Q. Is air a fluid?

A. I beg your pardon?

Q. Is air a fluid?

A. Air is a fluid, water is a fluid, that's why when I mention water, I said liquid water because water can be vapor, liquid or solid ice. There are three phases, yes.

Q. And you have a slide about rockets?

A. Right. It shows here the space shuttle taking off and the hot gases from the engines coming out. What you see in that picture I would say right away it's turbulent because there are many eddies. Eddies is like a swirling part of the fluid rotating and turning with different sizes. And once you see that, that's a turbulent flow.

Q. And are there eddies present in fluid sometimes that you can't see with your eyes?

A. Yes, there are many in the room. If this ceiling is about 16-foot high, I would say the largest eddy here would be at about two to three feet, one meter, and it goes down to smaller than a millimeter.

So it's like a Russian doll, you have big eddies containing smaller medium eddies, and so on, depending on the flow rate, yeah. This was discovered by Da Vinci,

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Leonardo Da Vinci in 1500, so it's not a new thing.

Q. I will move forward in your slides to that part.

A. Right, that's -- yes.

Q. So you said that Leonardo Da Vinci made some observations about turbulence?

A. Absolutely. Yes, he is the one that created the word "turbulence." Many Italians called turbolenza, which is written there.

Q. So is turbulence a newly discovered phenomenon?

A. No, it existed all -- the first person who really looked at it carefully was Da Vinci.

Q. All right. And you had another couple of slides here?

A. Right. Simple experiments in the river, he puts a plate across the flow, and he looked at what you see there are Eddies of different sizes coming out of the plate, yes.

Q. All right. And this is another drawing you --

A. Right, yeah, that picture appears in many books and turbulence because it's the first thing that showed Eddies of different sizes, yes.

Q. And can you draw on the screen in front of you which parts there are Eddies?

A. Okay. So, oh, wow. That's good. And so let's see, these are big Eddies, and medium Eddies and then tiny like this, and much smaller, yes.

Q. Okay. And in your work, you studied the movement of

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A. Yes.
Q. And that's 43 degrees Celsius; is that right?
A. Correct.
Q. And it also says the air temperatures reaching the patient are approximately two degrees centigrade lower than the listed temperatures; is that right?
A. Correct. We use 31 or 41.
Q. 41 degrees?
A. Yes.
Q. Do you know if that's the same temperature that 3M used in doing their work on this matter?
A. I didn't look at their work. I didn't, yeah.
Q. Now, you modelled some draping in your work?
A. Correct.
Q. And what import, if any, was the draping in the model that you did?
A. Okay. Before we did the work, we went with counsel to a surgery room in Santa Monica, California, orthopedic surgery hospital, and we asked the nurse to set up the Bair Hugger blanket, drape, as she usually does in an operating room. And we took one of our colleague of the lawyer, she's a lawyer, and we asked her to lie down on the operating table covered with the Bair Hugger blanket, tied the things, and covered the drape, and we asked the nurse to turn the Bair Hugger on. And we asked the lawyer on the bed whether

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there's air coming toward her face, and she said, no, because she has contact lenses and if the hot air is coming to her eye, she would stop the thing. So she said no air coming up. So we went around, there were other lawyers. We looked at the airflow and all the air was coming at the edges of the drape.
Q. All right. Have you seen one of these before?
A. Correct.
Q. And what is this?
A. It's a blanket that should be connected to the Bair Hugger with a hose.
Q. All right. And when you went to the operation, the operating room?
A. Correct.
Q. In Santa Monica?
A. Yes.
Q. Was there anything over this?
A. Yes, it's the same thing, yes.
Q. Was there anything placed on top of the blanket?
A. The drape, it's a plastic drape. The nurse put it on. That's how they keep, yeah.
Q. All right. And were those part of the assumptions that you made as you were --
A. Right. So from what we saw, we know the flow rate coming from the blower, and we divided equally to the edge

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of the drapes so uniformly coming to keep the mass flow rate the same, yes.
Q. Okay. So have you been asked to evaluate the effect that the Bair Hugger has on movement of particles in an operating room?
A. That was the main object of all the work, yes.
Q. And are you prepared to explain to the ladies and gentlemen of the jury what your work was with respect to the Bair Hugger and the CFD you did?
A. Okay. So after --
Q. Could I stop you for just one second?
A. Yes.
Q. Thank you. Do you have an opinion that you hold to a reasonable degree of engineering certainty about the effect of the Bair Hugger machine on the disbursement of squame size particles in an operating room?
A. My opinion is based on our results.
Q. All right.
A. I had no opinion before because of Navier-Stokes you cannot guess about it. After we did the computations, I can say now, that, yes, the Bair Hugger causes squames to arise from the floor to higher elevation.
Q. All right. And does that include over the operating room table?
A. Correct.

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Q. And also to the surgical site?
A. Say that again?
Q. Does your model also show squames reaching the surgical site?
A. Yes.
Q. So what did your LES model include in the operating room? Are there squames?
A. Right. So after we did the geometry as shown by 3M, we said the boundary condition from the drape, and in order to give 3M the best case scenario I mean in their favor, we put the squames only on the floor, not anywhere in the room, about one centimeter from the floor, so we put a layer around the operating table with three million squames.
To give you an idea, each human being sheds 20 million squames per hour. Think of that, that's a lot of squames. And if you have five people, they shed hundred million squames per hour. To follow these squames, all of them with the correct way we do it would be very expensive. So we put only three million on the floor, only three million. And if you look from the top you look on the table, the operating table, the squames are taking a U-shape, means one side of the bed, one side of the bed, and one side near the Bair Hugger. And we -- these are stagnant, they're not moving, and we turn the blower on. We follow them. Each one we follow, each individual squame,

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there's an equation to describe the motion of each squame, and we followed that. It will give you a trajectory where each -- so I give them a color code. I give green, red, and green, red then yellow just to see the turbulent mixing how it will affect, so you can see I think there's a video that shows some of them go from the green side to the yellow side or red side and so on, to monitor them.

Q. Doctor, so the colors of the squame in your model, is that just so that we can visualize?

A. Absolutely. It's only for visualization. The color has no effect on anything. Only the size of the squame, and it's mass and density.

Q. And so the super computer, what does it do with the particle? I think you explained to the jury it calculates where it moves?

A. Right. So in addition to what we do with Navier-Stokes equation to tell you the velocity and the pressure and the temperature each point in the operating room, simultaneously, you saw the motion of each of the three million squame to see where they go.

Q. So the computers are doing the Navier-Stokes equation for each one of the three million squames?

A. No, Navier-Stokes only for fluid motion. If you have the -- squames have the density like liquid water, so think of them as very tiny rain drops. Navier-Stokes only

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applies to a continuum fluid means the molecules 22 to the 10 in one centimeter cube. That's just one fluid. Particles are foreign objects like oranges. They have their own equation, which took 150 years to develop, so we solved that equation individually to each squame.

Q. So you solved that equation for each one of the three million squames?

A. We saw that every microsecond three million. That's why you need a super computer. You can't do it on a laptop or some other machine.

Q. How long did it take the super computer to this?

A. If the machine is running without interruption, it takes about 10, 12 hours. It will take 200 years if you want to do it in other machine.

Q. Okay.

A. Yeah.

Q. Which super computer did you use?

A. The one in University of Texas at Austin.

Q. All right. Can anybody use the --

A. No, no, in order to have access to these machines, you have to write a proposal to a National Science Foundation to tell them I would like to solve this problem. It will be a peer reviewed by five people around the country, again, confidentially, and when they see that your work deserves to use a super computer, they will let you do that. Okay.

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Q. And your work here in this case was done on the super computer, right?

A. Correct, yes.

Q. Did you do a model with the Bair Hugger on and the Bair Hugger off?

A. That is essential. In order in science to see the effect of something, you have to show without and with, then you see the difference.

Q. And what, if anything, did you learn from doing the CFD LES with the Bair Hugger off?

A. With the Bair Hugger off, the airflow from the ceiling scavenges everything in front of it, and the flow exits from the floor, exit grilles near the floor.

Q. So did you see that the airflow was effective?

A. Yeah, we can follow, yeah, we can follow, yeah, uh-huh.

Q. Okay. Do you recall what mass flow rate you used in solving these equations?

A. Mass flow rate from the ceiling or from the Bair Hugger? There are two.

Q. From the Bair Hugger?

A. I don't recall. It is given somewhere in a table. We use that from Bair Hugger, yes.

Q. Do you know if it was from a 3M document?

A. Yes. I recall I think we used a little bit lower than what was written by few percent.

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Q. Do you know if you used the same mass flow rate as 3M's witness?

A. Again, if you're referring to the video of 3M, they had a table that would probably use the same, yes.

Q. And did the LES CFD that you did on the Model 505 generate videos?

A. Correct.

Q. And is that something that this super computers typically do when you do this kind of work?

A. Not typically, but you ask them to do it like after you, after you do the simulation, you save certain parts in a given time period, you store them, and then you run a video generating code using your data. So the video is -- remember, when you have hundreds of millions of points in the mesh, the mesh will have tens of million, hundreds of million, you cannot read the results at each point. It's impossible to read in time every microsecond of flow changing, so the best way to visualize that is to create a video to tell you how everything is moving, yes.

Q. And is that something that you do with some regularity in your work?

A. Right, right. That's the way to do for DNS or LES because the amount of data is huge, yes.

Q. All right. And do you know was the super computers that you worked on or that you used for this, were they

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functioning properly?
A. Of course. I mean otherwise, they will tell us if they're not. You get an e-mail every time something the machine has stopped for maintenance, they always tell you, yes.
Q. Were the equations that you used for your LES accurate?
A. Yes, yes, definitely, yes.
Q. And were the equations completed by the super computer?
A. I didn't hear the last verb.
Q. Was your work complete? You finished the equations or the super computer finished the equation?
A. Right, of course, right, yes.
Q. And would you consider the data that was generated by the super computers to be reliable?
A. Absolutely, yes.
Q. Does that include the videos that the super computer generated?
A. Absolutely, yes.
Q. And would that help you to explain to the ladies and gentlemen of the jury the effect of the Bair Hugger Model 505 on an operating room?
A. Yes.
THE COURT: We're going to take a 15-minute recess.
(11:08 a.m.)

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(11:27 a.m.)
THE COURT: Ms. Zimmerman, you may proceed.
MS. ZIMMERMAN: Thank you, Your Honor.
BY MS. ZIMMERMAN:
Q. Dr. Elghobashi, before we took a break, you were I think preparing to explain to the ladies and gentlemen of the jury how the supercomputer has generated videos summarizing the work you did in this case. Is that right?
A. Correct.
Q. And I'm going to turn your attention here, this is Plaintiffs' Exhibit 1612, slide 18, and it's a -- do you know what this is, Doctor? Is this one of your videos? Do you recognize the video, Doctor?
A. Yes. I'm sorry, I was not listening. Yeah.
Q. That's okay. And is this a video of your LES simulation with the Bair Hugger off?
A. Correct.
Q. All right. And I'm going to hit play, and if you can explain to the ladies and gentlemen of the jury what they're seeing, that would be helpful.
A. So there is a view of the operating room where the ten grilles and the ceiling and four grilles near the floor and operating table with four medical staff. The yellow, the green, the red right now it's spreading but originally they were in a U shape around the operating table. Each color

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has one million squames. And what you see in time in the trajectories or where each individual squame is at a given time, now you see all the spreading and turbulent mixing allows them to cross, go from right to left, because the eddies can go any way depending on flow conditions in there.
Q. And what, if anything, from this video, is relevant to your opinion about the movement of particles in an operating room?
A. Oh, I think you can see that none of the squames reached higher than the shoulder of the medical staff, sometimes near the waist. Of course we have other visualization that we, routine, that shape to see exactly the details, but this is one of the -- one of the angles. I think in an original report there were different angles.
Q. All right. And did the supercomputer generate multiple videos for you?
A. If you wish, you can ask -- you can run a visualization program that takes the data from LES in a given period of time to create a video, yes.
Q. Okay. And did you also have some of these videos made to show what the effect is with the Bair Hugger on?
A. Correct. That will be this one here. Before it starts, you can see the yellow, green, and that's the initial position of the squames before we turned the Bair Hugger on, yes.

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Q. So each of these -- each of the colors on the bottom, those are -- those represent squames?
A. Each color is one million squames.
Q. And are they -- are they --
A. The -- excuse me. But the squames, think of a little water droplet, the size is about ten microns. And usual human hair, if you look at one of your hairs, it's about a hundred microns, one tenth of a millimeter. This is one tenth of a human hair approximately. Of course hair can have different sizes. So these are tiny particles and their density is like water because people know, the human body has 75 percent water, so when you shed skin squames, these have the same density as water, yeah.
Q. And each of the squames is ten microns in your --
A. Correct.
Q. -- model?
A. Correct.
Q. All right. And then this is the video of the Bair Hugger model 505 on?
A. Right, yes.
Q. And what do you see here?
A. The squames rise at a higher level than the previous video, and you can see that, very obvious.
Q. The people in your video are not moving. Is that right?
A. Correct.

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Q. All right. What impact, if any, would there be if the people were moving?
A. It would be much worse. I mean, I summarize first, all the simulation we did, we did everything in the simulation to provide the best case scenario for 3M, not for us. I wanted the best case scenario. I wanted to see, put everything on the floor, because in general, in a operating room, the squames are everywhere. We could have put them one meter high, two meter, we put them near the ceiling, then they will drop, but we did not do that. We put, again, best case scenario for 3M. So these came from the floor up only if the Bair Hugger is on, yeah.
Q. Doctor, as you were preparing your work in this case, did you review an article by Dr. Memarzadeh? Does that name familiar?
A. A long time ago, just somebody told me there is a person at NIH who did something and related. I looked at it and I think he was using RANS, R-A-N-S, which, as I described earlier, is the lowest level of simulation, means untrustworthy for this load. You can use RANS for a garden hose, that's okay, but you use it for this, that's bad, bad idea.
Q. Doctor, do you remember what size particles Dr. Memarzadeh --
A. Ten microns.

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Q. The same size you used?
A. Yes.
Q. And he used the RANS model. Is that right?
A. Yes.
Q. Did Dr. Memarzadeh include a drape in his --
A. No.
Q. And what impact, if any, does that have on the results?
A. Well, we tried to put everything in the operating room as I saw it by myself in the Santa Monica operating room. That's the nurse told us this is how we do orthopedic surgery, so I followed that.
Q. Do you know, did Dr. Memarzadeh, did he conclude that particles reached the surgical site as well?
A. I could not hear what you said.
Q. I'm sorry, I'm not speaking into the microphone.
A. Oh, okay. Okay.
Q. Let me direct you, the book in front of you, Plaintiffs' Exhibit 1419, page 3.
A. Yes.
Q. And the first full paragraph, did you start out discussing Dr. Memarzadeh's work?
A. Correct.
Q. Do you know how -- he used a RANS model. Is that right?
A. Correct.
Q. Do you know how many particles he modeled?

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A. I don't remember, maybe 3,000. It could be written here somewhere.
Q. 4,000 sound right?
A. 4,000, okay.
MR. BLACKWELL: Objection, Your Honor. Leading.
THE COURT: It is.
MS. ZIMMERMAN: All right.
BY MS. ZIMMERMAN:
Q. The fifth line down in the first full paragraph.
A. Okay. Yes.
Q. And I'm going to direct your attention about midway through the paragraph.
A. Yeah.
Q. And your paper says, it's the sentence starts out they. Do you see that?
A. Yeah, they, the first word in the sentence they, upper case they.
Q. Could you read that to the ladies and gentlemen of the jury?
A. They showed that roughly 2 percent to 5 percent of particles reach the surgical site, and in italics, provided they are originated very close, about 1.3 centimeter above the site, yes.
Q. Okay. And your particles started where?
A. On the floor, yeah. We avoided anything, yeah.

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Q. Did Dr. Memarzadeh's group use a drape?
A. I don't think so, no.
Q. Okay. And why -- why might a drape matter?
A. Again, go back to Santa Monica hospital, we had to do the conditions in a operating room identical to what happens in reality when you have a surgery, so I did not omit anything, except some insignificant machines, computers and things which are not really important.
Q. Okay. Tell me about that, Doctor. You -- have you seen pictures of the operating room that was where Mr. Gareis's surgery took place?
A. I think the during the deposition the counsel of 3M showed me photographs of a operating room called Providence. I don't know what it is. But he showed me the machines and yes.
Q. Okay. And, in your model, did you include a patient?
A. Include a patient?
Q. Yes.
A. Yes.
Q. Did -- what about a surgical team?
A. We have four, four surgical team people.
Q. What other equipment did you use in your model?
A. Well, the Bair Hugger surgical masks, and that's it.
Q. There have been some questions to other witnesses about other devices used in that operating room. Do you know what

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Q. Just yes or no, sir.
A. I disagree. Your question is not like that. You're saying that the dimension of the grille, the four grilles in the floor taken from 3M geometry, the ten grilles in the ceiling, these were taken from either from 3M geometry or Rochester, when you go to a operating room, we visit all of them, they have different grilles like the one you mentioned, Providence, so you want me to simulate all operating rooms in the world?
Q. No, sir, I just want to know when you received information from the lawyers when you did any homework or research yourself to --
A. A lot.
Q. -- independently verify?
A. I did a lot.
Q. What did you do, for example, to --
A. Looking at geometries and ventilation system of -- by HVAC people. There were journals. I spent many, many hours trying to get that, finally decided that all operating rooms have different inlet, outlet, like the one in Providence, so I took the best case scenario for 3M. All the outlets on the floor, that's the best case. If you lose outlet, you will have more squames out, trust me.
Q. You were asking, sir, for the locations of inlet and exit air grilles --

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A. Yes.
Q. -- as pertained to Mr. Gareis in the hospital in this case? What did you do to verify that the information that you got was accurate?
A. Mr. Goss showed me the grille location in Providence operating room, and I told him, and I repeat again, the location of the grille on the wall at the higher elevations of the floor increases, enhances the dispersion of squame toward the table because that allowed the plume of the 505 to rise higher. If the grille were down, air would -- incoming air would push the heated air down. If you -- if you put all the outlet grilles higher, you would have a much worse operating room.
Q. So I think I've gotten about the best answer I'm going to get, so I'm going to move on and ask you another question.
A. Okay. All right. Good.
Q. So you made the statement awhile ago when the other lawyer was standing here that all the other machines in the operating room had less watts than the Bair Hugger machine. Who told you that?
A. I looked in it the web about the different machines in a operating room, including an anesthesia machine, the cauterizing machine, the all of that, computer, for example, the fan of any computer produce like ten watt or something,

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very small, computers in operating room has nothing, all other devices that use intermittently for few seconds or minute will have no impact, in addition, any electric device that generates heat with a fan will create its own plume. If you have many plumes in the room, it will be the worst case scenario for 3M, so I did not. I wanted to have a pure operating room that you not raise any issue about it, trust me.
Q. Do you recall what my question was, Dr. Elghobashi?
A. I don't recall the question.
Q. It's true, isn't it, that you're not able to tell me or the jury or anyone what the make or model or any of the details or specifics were for any piece of equipment that was, in fact, in the operating room for Mr. Gareis on the day of his surgery on November 9th, 2010, that's true, isn't it?
A. I totally agree with you.
MR. BLACKWELL: I'm going to switch gears, Your Honor.
THE COURT: Actually, we'll take lunch break and resume at 2 o'clock.
(1:07 p.m.)
* * * * *

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PROCEEDINGS
(2:09 p.m.)
THE COURT: Please be seated. And Dr. Elghobashi, you're still under oath from this morning. And Mr. Blackwell is going to resume his questioning, whenever he's ready. Are you ready?
THE WITNESS: Yes.
THE COURT: All right.
BY MR. BLACKWELL:
Q. Good afternoon again, Dr. Elghobashi.
A. Good afternoon.
Q. I hope you had a nice lunch.
A. Thank you.
Q. I want to go back to the testing you did of the Santa Monica that you talked to us a little bit about.
A. Yes.
Q. And I believe it's true that you had never before seen a Bair Hugger set up in an operating room at the time of the experimentation you did out in Santa Monica; is that right?
A. Correct.
Q. So is it true then that the persons who actually set up that operating room and arranged the whole thing were, again, these lawyers; is that right?
A. Could you repeat the question again, please?
Q. The persons who set up the visit to the operating room

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Q. So let's bring this back to the operating room number 4 at Providence Hospital Northeast in Columbia, South Carolina, where the surgery took place on November 9, 2010. Now, were you aware that there was an opportunity for experts like yourself to come out to the actual operating roo Mr. Gareis had been i to take your own measurements. Did you know that?
A. I will repeat what you told me, just to make sure I understood. You said I could have gone to whatever this other hospital is and take measurements and I said earlier I don't trust in taking measurements the way you propose so why would I go to place to do something that is illogical to me? It doesn't make sense.
Q. Let me ask my question again because I don't want to argue with you.
A. Okay.
Q. I just want to know whether you were aware that there was an opportunity for an expert like yourself to come out to the hospital where the surgery took place and either take measurements or have measurements taken. Did you know that?
A. I have not known that.
Q. So to the extent there was a meeting set up for that purpose, is it fair to say that you weren't invited to the meeting as far as you know?
A. I was not invited to a meeting in the Carolinas.

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Q. Now, when you were finally able to see the actual photographs of operating room number 4, and you said Mr. Goss showed them to you?
A. Yes.
Q. There is Mr. Goss?
A. I met him in the morning.
Q. And he showed them to you, and at the time he showed you those photographs, didn't you ask the question how come these photographs weren't shown to me before today. Isn't that what you asked?
A. My memory is not very good, but if it was written that I said that, then I trust you. I cannot remember. I mean I have so many things.
Q. I'm okay, I'll do trust to verify. So if you could look in your big binder we have up there.
A. Oh.
Q. And look your deposition for February 10th of 2018.
A. Okay. I have it.
Q. And then go to page 226 and lines 22 through 25 on page 226?
A. I have -- I have page -- the page has four pages. The one page has four squares, right?
Q. If you look at the square that has the 226 in the corner.
A. Okay, I have it.

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Q. Okay. And lines 22 through 25.
A. I do.
Q. And do you see where the question is asked -- where you ask --
A. Yes.
Q. -- how come they didn't show me these pictures before today?
A. Right.
Q. What did your lawyer say? Would you read that for the ladies and gentlemen of the jury?
A. Because they are irrelevant.
Q. So when you asked how come you didn't see the pictures before today, it was the same lawyers who are telling you that the pictures that show the actual operating room are irrelevant, that's what they said?
A. That's what's written here, yes.
Q. And that's what you heard?
A. I don't remember but it's written, means I heard it, yes.
Q. So in any event, had Mr. Goss or 3M not shown you the photographs of the operating room, for all you know you'd never have seen them, right?
A. Correct.
Q. Now, going to another subject, Dr. Elghobashi. The jury has heard some references already that relate to the

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movement of personnel and in out of the operating room and the significance of that. Do you understand that the movement of personnel in and out of the operating room is an important risk factor for surgical infections? Do you know one way or the other?
A. I'm not a medical doctor.
Q. Now, I think you told us before that none of the personnel that you had depicted in your CFD move?
A. Correct.
Q. If the -- at least assume for purposes of my question that the international consensus of orthopedic surgeons has a statement, persons in the operating room are a major source of bacterial load and shed bacterial particulates. These particulates circulate through the operating room via air currents. Movements of personnel and objects, including operating room equipment and opening and closing doors, can generate significantly marked air currents and increase the probability of bacteria being deposited in the surgical site. So I take it given your answer that you are not a medical doctor, then you don't have any basis to disagree with the international consensus of orthopedic surgeon on the significance of the movement of personnel and object in the operating room?
A. I agree on parts of this that does not mention infection. If you open the door or let the people move, you

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will enhance the spreading of squames. I'm not talking about infection. So that's why I said all our computations were done as the best case scenario for 3M not our side.
Q. You keep repeating that. Are you --
A. Yes, I do.
Q. -- suggesting --
A. I do, I do.
Q. May I finish, please, sir? Are you suggesting to the jury that you are being paid over $250,000 to help 3M, are you trying to suggest that?
A. The science, what the science I perform to prove to show these results, I could have picked moving people easily. I could have opened/closed the door and the squames would have been risen at a much higher rate than what I did, so I did the one -- you mentioned the money. Don't mention the money. I don't care about the 250, that's just nothing.
Q. You don't care, it's nothing?
A. Absolutely nothing for because it's paid to students.
Q. Dr. Elghobashi, if what the jury wants to get is an accurate picture of the nature of squames or particles or bacteria.
A. Yes.
Q. Taking into account all of the factors that may have contributed to it in the operating room, we can agree that your CFD does not depict that, true?

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A. I repeat again. If we allowed the people to move and the doors to open and close, the Bair Hugger effect would have been enhanced in spreading squames. So we did it such that just to isolate the effect of the Bair Hugger, that's how we do science.
Q. With all due respect, sir, you're not answering my question. If the jury wants to understand all of the factors in the operating room that might affect the air currents, the movement of squames or particles or bacteria, your CFD does not encompass or include all of the factors that would contribute to air movement occurrence in the operating room. Is that true?
MS. ZIMMERMAN: Objection, Your Honor. Asked and answered.
THE COURT: Overruled.
BY MR. BLACKWELL:
Q. Is it true, sir?
A. I answered my answer which is the correct answer for me. I cannot answer any more. What do you want me to do?
Q. I would like you to tell me if it's true or not true, sir?
A. Which is what is true and not, could you repeat it again?
Q. I will try one more time.
A. Yes, please.

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Q. If the jury wants to understand all of the factors in the operating room that would contribute to the movement or air currents and/or the creation of squames or particles, Mr. Gareis's operating room, your CFD does not take into account all of the factors that would have contributed to the movement of air currents in the operating room. That's a true statement, isn't it?
A. I disagree. And you want me to explain to you why, I will do it. I disagree with that statement, yes, I do.
Q. Well, let me ask you then this way. If you say you disagree and you took into account all of the factors, isn't it true that in no respect whatsoever did you attribute any value to the fact that the doors to that operating room were opened and closed at least six times during the surgery of Mr. Gareis on November 9, 2010, you didn't factor in even one of them, did you, sir?
A. I did not account for any door closing or opening.
Q. Thank you. You answered my question.
A. Okay.
Q. Isn't it true that to the extent there's other equipment in the operating room that generates heat or blows air, you included not a single one of them in your CFD. Isn't that also true?
A. It is true but irrelevant.
Q. That may be your opinion. I'm just trying to understand

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what you did and what you considered. Isn't it also true, even though you said you were putting together the best case for 3M, that the patient that you had modelled in your CFD was a patient that had zero bacteria on his or her own body. Isn't that true?
A. Do you mean I made sure that our patient in the simulation is not sick?
Q. No, that's not what I meant.
A. If you have bacteria on something means it's not right. I did not -- I took a clean patient.
Q. All right. So a clean patient, you meant a patient that had no bacteria is what you took, true?
A. We do not account for bacteria because they are much smaller than the smallest turbine scale.
Q. Sir, I'm trying to understand what you assumed. So when you say that you took a patient that was cleaned or whatever word you used, you presume to have a patient in your CFD that contained no bacteria on his or her skin, that's a true statement, isn't it?
A. I disagree. The simulation does not account for bacteria at all, whether patient or floor or medical stuff, so there is no place to put bacteria in because bacteria is much smaller than the particle, the squames.
Q. All right. So fairness to your point, if there is no bacteria taken into account, that means there would have

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A. I think I remember, but I don't know. I mean, it's a different division.
Q. But you do know him as a scientist?
A. I never met him. I don't know him. I just read his paper. That's all. I have no idea who he is.
Q. And the paper you read was of a CFD?
A. Yeah.
Q. That he had done as an employee of the National Institute of Health involving the Bair Hugger, right?
A. Yeah.
Q. And now he published his results too from his study and came to a conclusion that's different from yours, didn't he?
A. It doesn't matter. I don't look at RANS papers.
Q. Sir, it --
A. It doesn't matter.
Q. It matters to my question so --
A. I don't remember what he said. When I see a paper with RANS, I just put it away. I don't read it.
Q. So you told us previously that you had read his paper, had you not? Did you not read his paper?
A. Oh, okay. When I read the paper, if it's high quality, I read it from front to end. If I open a paper and I see unacceptable method, I just look at the summary and stop.
Q. All right. So with respect to Dr. Memarzadeh and the criticisms you gave today on his methodology, isn't it true

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that you never wrote anything to either the National Institutes of Health or anyone else critical of Dr. Memarzadeh's methodology. Is that true?
A. Why would I write -- there are tens of thousands of paper published every year using RANS.
Q. Dr. Elghobashi, I'm just trying to understand whether you wrote your criticism to the National Institutes of Health, and sir, either you did or you did not?
A. If the paper came to me to review I would reject it, but since I'm not a reviewer and I'm not his boss, if I am his boss, I'll tell him don't it, but he did it so I have nothing to say.
Q. So Dr. Memarzadeh's paper was written in 2010, right?
A. Could be. I don't remember.
Q. Well, I'll represent to you that it was 2010 and assume that it was?
A. I accept your representation, yes.
Q. So that means he wrote his paper at least six years before you had ever even heard of the Bair Hugger, true?
A. I read the paper by Mr. Memarzadeh when the counsel asked me whether I would be interested in doing that work. So I looked at the literature and I saw that. That would be 2016. Why do you say 2010?
Q. It was 2010 that Dr. Memarzadeh published his paper.
A. Fine. If he did, that's fine. I have no problem.

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Q. And the fact is that you had no cause to make any criticism of Dr. Memarzadeh's work until after the time you had been retained to be an expert witness in this case. That's true, isn't it?
A. Sir, I disagree with everything you said.
Q. That's generally true today. So but my question is --
A. Can I explain, give you some history to help you? Imperial College of London created RANS model. My Ph.D. was in RANS, so I -- because 1974, '71, there were no computers to do DNS or LES. We have University of London computer was smaller than your laptop. So I have a Ph.D., '74, in one of the best schools in the world. We use RANS because RANS was created at Imperial College. Everybody know that. What I'm saying to you, do not use RANS in a complex geometry because it will fail. No person in the royal society of London, no person in the national academy of America will disagree with me. They know what I say. So I know RANS because I did my Ph.D. using it, okay?
Q. Do you remember my question, sir?
A. No.
Q. My question was whether you had had any cause to criticize Dr. Memarzadeh or his methodologies until after the time you had been retained as an expert by these lawyers. You had not ever criticized Dr. Memarzadeh before you had become an expert in this case. That's a true

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statement, isn't it?
A. If you insist, you can make it true, but I had no reason to read something I don't know about.
Q. Let me --
A. I have no reason to -- I have no reason to write to a person that I never read or know anything about him. I don't write to Chinese, to Japanese that use RANS, I don't do that.
Q. All right. So let me ask you about the conclusion he reached as you read the paper, where he said forced air warmers seem to cause minimum disruption to laminar airflow systems that help protect the surgical site from contaminated particles sourced from surgical staff. This investigation validates Moretti's conclusion that forced air warming technology does not increase the risk of surgical wound infection. That's what Dr. Moretti said, true?
A. If you read it, I agree with you, that's what you read, but it's rubbish because there is no laminar flow in an operating room.
Q. Good point. So to the extent anyone walks to the back doors of this court, comes in here and takes the stand and says there is such a thing as laminar flow that creates a force field in the operating room, that is pure rubbish, isn't it?
A. What's the last word?

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Q. Rubbish.
A. Absolutely. RANS number is ten thousand, there's no laminar flow.
Q. Right. So anybody claming there's laminar flow and it creates force field?
A. Right.
Q. It's not just rubbish, it's absolute rubbish?
A. Absolute rubbish, and I give an excuse because that person does not know turbulence.
Q. They don't know turbulence and they don't know what they're talking about?
A. No, because they don't know turbulence, they make silly statement.
Q. Okay. We'll take silly, silly statement.
A. Yeah.
Q. So I know the answer to this question, I'll ask it any way. You never had any desire to reach out and have a conversation with Dr. Memarzadeh about how his conclusions may differ from yours. Is that true?
A. Absolutely no interest. Absolutely no interest.
Q. Thank you, Dr. Elghobashi.
A. You're welcome.
THE COURT: All right. Ms. Zimmerman, anything else?

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REDIRECT EXAMINATION
BY MS. ZIMMERMAN:
Q. Good afternoon, again, Dr. Elghobashi.
A. Good afternoon.
Q. Mr. Blackwell asked you some questions about whether or not you did a CFD in the operating room where Mr. Gareis had his surgery. Do you remember that?
A. Correct.
Q. And do you have an opinion about whether the CFD that you did is relevant to the operating room that Mr. Gareis's surgery took place in?
A. I do absolutely, yes.
Q. How is it relevant?
A. We put in the operating room all the ingredients that would distinguish between the blower on or the blower off. We had the patient, the operating table, the Bair Hugger blanket, the drape, certain lights, people.
Q. Let me stop you for a second. What's this a photograph of?
A. It's an operating room with a patient on an operating table showing the knee of the patient and --
Q. Is that the draping you used in your model?
A. Correct.
Q. And so you were explaining to the ladies and gentlemen of the jury why you believe your CFD is relevant to

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Mr. Gareis's operating room?
A. Could you repeat the question again, please?
Q. Sure. Do you believe that the CFD, the LES that you did on the Model 505, is also relevant to the operating room?
A. Absolutely, no question.
Q. And how?
A. It has all the information needed to study the effect of a device, air warming device, in a room in the neighborhood of an operating table. And again, the room has 25 air changes per hour, four exit ducts, like, again, I know the 3M lawyer did not like that, but that's what the best scenario for 3M, the best. I could have added more things that would have enhanced the spreading of squames, absolutely. Any additional heating from a fan, from a machine will create its own plume that will resist the cooler air coming from the ceiling so it will be much worse.
Q. Are there any other heat sources in the operating room that have a greater heat source than the Bair Hugger?
A. I don't think so. I mean, the Bair Hugger had the more wattage than any other device running continuously. There are other devices intermittently used.
Q. And Mr. Blackwell asked you some questions about the assumptions that you made.
A. Right.
Q. And that those were from the lawyers like me. Is that

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right? Do you remember that?
A. Could you repeat? I don't remember.
Q. Mr. Blackwell was asking you questions about the boundary conditions that you did?
A. Oh, yes, yes, right.
Q. And Mr. Blackwell said that you got all of that information from the lawyers on the plaintiffs' side?
A. Oh, right, right. He mentioned that.
Q. I'm going to show you, this is Plaintiffs' Exhibit 1337, page 12, which is previously admitted. Does this show that the temperature at the end of the hose?
A. Right.
Q. Is 43 degrees?
A. Yes.
Q. And does this document tell you what temperature comes out of the holes?
A. No, it didn't. It just showed what the exit of the hose, at the end of the hose, that's what I told him.
Q. Does it say the air temperature is reaching the patient or approximately 2 degrees celsius lower?
A. Right. Yeah, and we did 41.
Q. And so that's from 3M's document?
A. Yeah, I tried to explain to him, yeah.
Q. And it also shows the BTUs, correct? What am I doing, I can touch my paper. Does it show the heat generated by the

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Bair Hugger?
MR. BLACKWELL: Objection, Your Honor. Leading.
THE COURT: Sustained.
MS. ZIMMERMAN: Withdrawn.
BY MS. ZIMMERMAN:
Q. You just had some questions posed to you on laminar airflow.
A. Yes.
Q. What is the difference between unidirectional and laminar airflow?
A. No connection whatsoever. Laminar, as I showed in the PowerPoint, means RANS number should be less than 2,000. Unidirectional flow means a flow in a garden hose going from left to right, that would be unidirectional. Laminar can be just anything that has a low RANS number. And in the operating room, some people call it uni direction just absolute nonsense. You've seen the videos, it's all eddies everywhere. There is nothing called unidirectional when you have a grille pushing air or anything into a room, nothing. The recirculation, I mean, we teach that for undergraduates.
Q. Did the LES that you did with the Bair Hugger off tell you anything about the effect of a unidirectional airflow?
A. There is nothing called uni direction. We put the airflow from ten grilles at so many meters per second or a fraction of that going down, and once they leave, they take

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their own behavior from equation, the turbulence will have --
Let's say this. If you have a garden hose one-inch in diameter connected to another garden hose three-inch diameter, we call this southern expansion, mean you can that in air conditioning devices or rockets or anything, it's a small pipe connected to a bigger pipe. Once the flow leave the little pipe, immediately at the edge of the junction you have recirculation.
So if you look at the ceiling, this is big room it's a big pipe and those little guys are pushing air immediately bubbles, we call it bubbles, recirculation is on, yeah, yeah, that's nothing, trust me, no unidirectional flow, none.
Q. All right. Mr. Blackwell asked you some questions about the timing of your report, do you recall that, and versus when this lawsuit was commenced?
A. I think he wrote some dates in by pencil April something, yeah, okay.
Q. And you don't know as you sit here today what other evidence the plaintiffs had, the plaintiffs' lawyers had?
A. No clue, I have no clue about these things.
Q. You don't know what kind of 3M documents we had when we filed those cases?
A. Zero. I don't have no brain for that.

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Q. Have you seen the pictures from Mr. Gareis's hospital in Providence?
A. Mr. Goss showed me?
Q. Yes.
A. Yes, I seen.
Q. Did the difference in the operating room that you've seen in the photos, do they change your view about whether or not the Bair Hugger Model 505 can take squames from near the floor and deposit them on the surgical site?
A. None whatsoever. None. Actually, if I had time or energy to do the other room in detail which it will much worse. All the squames would be rising at a much faster rate. For two reason. Number one, the airflow rate in the Providence Hospital at the grille, the RANS number is 6,000. The one we did in our thing, in our big room for 25 changes per hour produces RANS number between nine and ten thousand. That means the air coming from the ceiling, what we did for 505 is a stronger flow that scavenges everything in front of it. If I had done the Providence room, the lower RANS number, you would have seen the plums coming up very quickly.
Q. All right. It only gets worse?
A. I keep saying to him, he did not trust me, but I told him it's the best scenario for 3M, repeat it.
Q. All right. Now, Mr. Blackwell asked you some questions

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about a presentation that you did in Santa Barbara.
A. Yes.
Q. Do you recall that?
A. Yes, and I tried to explain to him that the picture, that what he presented was incorrect.
Q. And you wanted to explain why, correct?
A. I tried many times. He stopped me, yeah.
Q. All right.
A. I complain about that.
Q. Well, now is your chance. What did you want to explain to the ladies and gentlemen of the jury?
A. Okay. That lecture, it was five years ago, okay, Santa Barbara. That picture here shows on the left two lines, I think one red and one black.
Q. And you can touch the screen, if you want.
A. Okay. These two lines here are different color, all right. And let me, I mean, I'm going to have to reduce the jury to this, we have a figure, a graph, a plot of two lines. The axis, which is the horizontal line in the axis, called K, that gives you how big the edges are, okay. In the vertical line, it shows how much energy in each eddy. This eddy that comes from the room, some of them are stronger than others so energy -- and I have to say that plot, what we call the XCs, are on the log algorithm scale, log, log. And I'm sorry to mention these words, but it's

UNITED STATES DISTRICT COURT
DISTRICT OF MINNESOTA

Louis Gareis and Lillian Gareis, Plaintiff, v. 3M Company and Arizant Healthcare, Inc., Defendant.	VOLUME IX File No. 16-CV-4187 (JNE/FLN) May 25, 2018 Minneapolis, Minnesota Courtroom 12W 9:32 a.m.

BEFORE THE HONORABLE JOAN N. ERICKSEN
UNITED STATES DISTRICT COURT JUDGE

(JURY TRIAL - VOLUME IX)

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Proceedings recorded by mechanical stenography; transcript produced by computer.

PROCEEDINGS

(9:32 a.m.)

THE COURT: Good morning. Welcome back. Please be seated. Good morning.

MR. GOSS: Good morning, Your Honor. Your Honor, defendants call Michael Keen as our next witness.

(Witness sworn.)

THE COURT: Please take the witness stand, which is right there, and once you're comfortable, state your full name, spelling your last for the record.

THE WITNESS: Good morning. My name is Michael Keen.

THE COURT: Spell your last.

THE WITNESS: Oh, sorry. K-E-E-N.

DIRECT EXAMINATION

BY MR. GOSS:

Q. Good morning, Mr. Keen. My name is Peter Goss. I'm one of the lawyers for 3M, and I'm going to have a few questions for you this morning. Mr. Keen, where are you from?

A. I'm from Toronto, Ontario, Canada.

Q. Okay. And Brett, can we bring up slide number 1, please?

Toronto, is that north or south of here?

A. Ironically, it's actually southeast of here.

Q. Okay. Well, thanks for coming up from Canada. Where do

you work, Mr. Keen?

A. I work at a group of hospitals in Toronto, St. Michael's, St. Joe's, and Providence Health Care.

Q. And over the course of your education, training, and experience, have you developed expertise in hospital engineering?

A. Yes, I have.

Q. And does that include heating, ventilation, and air conditioning, or what we might refer to as HVAC, in hospitals and health care facilities?

A. Yes, it does.

Q. All right. Brett, could you pull up slide 2, please?

I'd like to review your education briefly. You were an undergraduate at the University of Waterloo. Is that in Ontario, Canada?

A. It is Ontario.

Q. And you received a bachelor of science in mechanical engineering. Is that right?

A. Bachelor of applied science in mechanical engineering, yes.

Q. Thank you. And then you went on to pursue an MBA at Queens University, also in Ontario; is that right?

A. Yes, that's right.

Q. Were you working during the time that you received your MBA?

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than the air that's coming down here.
THE COURT REPORTER: What was the last part?
THE WITNESS: 30 times stronger than the air that's coming down the operating room.
BY MR. GOSS:
Q. So a hair dryer is that much stronger than the velocity specified in 170?
A. Yes, that's correct.
Q. Okay. Now, this drawing, you mentioned that it just has the surgical table, there are no people or equipment in it, is that what the airflow pattern would look like when you put the equipment and the people in?
A. No, this is an idealized sort of schematic of what you're trying to achieve. Once you start to introduce people, equipment, any other obstruction, that sort of unidirectional downward flow starts to get disrupted by those things.
Q. Okay. So what are some specific examples of equipment and other things that would be in that flow over the operating table?
A. And the other things, like I mentioned, that hang from the ceiling, the operating lights are sort of a big obstruction that the air hits probably first. There's often monitors on arms that are hanging from the ceiling as well that the surgeons are looking at these monitors. Those are

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in the sort of field as well. The people themselves, the operating room staff, as they move around the space, as they're working in this space, their obstructions to that airflow as well, and then ultimately the patient on the table.
Q. Sure. In your report, did you provide some examples from an article of about flow obstructions in operating rooms?
A. Yes, I included a list in my report.
Q. Okay. Brett, could we take a look at 436-12, please? Yes.
Is this a picture from an article you cited in your report?
MR. FARRAR: Your Honor, objection.
THE COURT REPORTER: I'm sorry, I didn't hear you.
MR. FARRAR: Objection. Hearsay on publishing.
THE COURT: We take it down for the moment?
MR. GOSS: Okay. I'm sorry. All right.
BY MR. GOSS:
Q. So you reviewed an article that addressed flow obstructions over the airflow table -- over the surgical table?
A. Yes, I did.
Q. Okay. And did that inform your opinions in this case?
A. Yes, it did.

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Q. And would it help explain your testimony to show the jury one of the pictures from that article?
A. Yes, it's a good illustration.
MR. GOSS: Okay. May we publish?
THE COURT: You may.
MR. GOSS: Okay. Thank you.
MR. FARRAR: Same objection. I don't know where it's coming from.
THE COURT: That's a good point. Could you tell us, maybe you did already, but where is this from?
THE WITNESS: This is a picture that I included in my report and I had the reference in the report. I believe this one might have been from a Price Industries Manual that I took. It could be off there. I'd have to check.
Q. We'll take it down. I believe it's from a white -- let's just take it down. That's all right. All right.
So you mentioned that the airflow velocity of 25 to 35, how did you characterize it?
A. Low velocity.
Q. Okay. Why would you want the velocity to be low if the goal is to clear particles from the room, wouldn't you want it to be high?
A. Certainly if your goal was just to wash away any particles and then have them exhausted from the room, the higher the velocity, you would think that that would be the

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best scenario to wash that away, but we're trying to balance with other circumstance, and the one circumstance we're trying to balance with is the patient on the operating room table has an open wound and you want to make sure that you have a velocity enough to wash away particles from that area but also you don't want to be, you know, slamming particles into an open wound as well with a high velocity.
Q. Okay. And does the patient's open wound, is there -- is it generating heat?
A. Yes, it is.
Q. Okay. And so does that have an effect on the air over the patient's wound?
A. It does. I mean, the patient's wound has a temperature, the body temperature, right, and that has heat involved with it, and so when you have an open wound, in the wound there's a thermal plume that comes off of that wound from the heat of the body temperature.
Q. And in your report, did you prepare a drawing to illustrate the thermal plume that comes from the patient's surgical wound?
A. Yes, I did.
Q. All right. And would that aid in presenting your testimony and opinions to the jury this morning?
A. Yes, I think it would.
MR. GOSS: Your Honor, we request permission to

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publish his graphic from his report.
THE COURT: Mr. Farrar.
MR. FARRAR: No objection.
THE COURT: Okay.
BY MR. GOSS:
Q. Brett this is page 43617.
All right. Is this the drawing you prepared?
A. Yes, it is.
Q. And can you just explain to the jury what that shows?
A. So this depicts what I just explained, so you can see the lines coming from the ceiling, that's the airflow coming from the vents above and you can see how that airflow comes down and washes over the patient in the operating room table. That's the blue lines coming down. You can see the patient on the table in the middle. So I've illustrated sort of where the open wound might be in the middle of the patient. The red lines coming up would indicate that thermal plume that's coming off of the wound site.
Q. So what does all of this have to do with the airflow velocity from the ceiling supply?
A. So as I mentioned from a velocity standpoint, you want to have enough velocity so you're actually, you know, bringing the air down, washing particles away from the patient on the table, but at the same time you don't want that velocity to high so it's not slamming particles,

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overcoming that thermal plume that's the natural barrier to protect the patient wound. You don't want to have velocity too, it overcomes that and throws particles into the wound.
Q. So is what you just explained, is that -- does that relate to the ASHRAE 170 standard for airflow velocity?
A. Yes, the velocity range that's in 170 of the 25 to 35 feet per minute was chosen to reflect this situation.
Q. And when the committee met to discuss this velocity and the right, I guess I would think of it as the Goldilocks velocity, not too slow, not too fast, what work were they -- or what was the basis scientifically for the decisionmaking?
A. Sure. There was a study done on this effect by one of the members of the ASHRAE committee. Dr. Farhad Memarzadeh did a study that looked at various characteristics of an operating room and what was ideal for the conditions to balance the washing away of particles and the defenses of the thermal plume.
Q. Who is Dr. Farhad Memarzadeh?
A. He works at NIH. He's a member of our ASHRAE committee.
Q. Do you know him personally?
A. Yes, I've known him since 2003.
Q. Okay. Is he -- do you consider him an expert in computational fluid dynamics?
A. Yes, I would.
Q. All right. And did he present his findings from his

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research to the committee?
A. He did. He presented at the committee. The committee had a chance to ask him questions, to debate about the findings that he had in his study, and then we ultimately made decisions based on the study and the discussions that we had as to what to include in the standard as a requirement.
Q. I want to turn now from the supply air to the exhaust vents. Does ASHRAE 170 have a requirement for exhaust vents?
A. Yes, it does.
Q. Okay. And this is the ASHRAE standard.
Brett, would you please pull up slide 7?
MR. FARRAR: Same objection for the record, Your Honor. Hearsay.
THE COURT: Overruled.
BY MR. GOSS:
Q. All right. And does this provision address the ASHRAE requirements for return vents in operating rooms?
A. Yes, it does.
Q. Okay. And so what do the return vents, where do they have to be to meet ASHRAE 170?
A. There needs to be a minimum of two exhaust vents in the operating room at two opposite corners of the room as far away as possible from each other, at a low level, about

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eight inches off the floor.
Q. Okay. And what role do return vents or exhaust vents play in clearing particles from the operating room?
A. Well, I mentioned before the fact that an operating room has that 20 air changes per hour. The idea there is to, you know, bring in clear air and to remove any particles, remove any dirty air from the operating room. And so the exhaust vents, that's where the air leaves the room so at 20 times per hour.
Q. Can you explain to the jury the difference between passive and powered exhaust vents?
A. Sure. A passive vent would be one that's just an open grill with, you know, nothing behind it. A powered vent would actually have fan that's behind those grilles somewhere down the line that's actually pulling the air out.
Q. So what kind of vents are typically in operating rooms, are they passive or powered?
A. They're powered.
Q. Okay. In your experience, 25 years of visiting operating rooms in Canada, the United States, other places, have you ever seen an operating room that didn't have powered vents?
A. No, I've never seen one.
Q. I want to turn now to -- Brett, can you take that slide down, thank you. -- to another ASHRAE 170 requirement and

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Q. And what forced air warming device was used in that study?
A. As I recall, the Bair Hugger.
Q. Now, he says that he's going to use particle tracking methodology. Did Dr. Elgobashi claim to be using a particle tracking methodology also?
A. Yes.
Q. And they're going to study whether or not there's an increase in the risk of nosocomial infections?
A. Correct.
Q. And nosocomial infection again is a hospital acquired infection?
A. That's my understanding.
Q. Now, they said that the NIH, the National Institute of Health, analyze laminar airflow disruption and room airflow patterns to determine the effect of squames impingement from personnel surrounding the operating table as the source of surgical wound infection.
A. How does that differ from Dr. Elgobashi's CFD model and the assumptions that he made.
A. Well, I don't believe he had squames from the personnel surrounding the table. So I think that's an item he omitted.
Q. Now, if we look on, it says Memarzadeh used advanced numerical modelling and empirical data to evaluate the

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effects of room parameters on minimizing surgical site contamination risk from specific particulate sources. What is meant by room parameters?
A. I would have to look at the paper that they're referencing because they're referencing a study, but as I recall there was heat, heated equipment in the room, and flow rates of air into the room and things like that.
Q. So it's stuff in the room that effects airflow?
A. Correct.
Q. Now, if you look just a couple more on the far right column in that first full paragraph where it reads, "the squame lots show that particles are cleaned away from the patient by the airflow from the laminar diffuser no matter if the forced air warmer is on or off," do you see that?
A. Correct.
Q. Is that consistent or inconsistent with your CFD and your CFD validation?
A. It is consistent with my work.
Q. And it says, "the percentage of squames deposited on the patient was zero, both when the forced air warmer was on or off." Is that consistent or inconsistent with your work?
A. Consistent.
Q. And, finally, they reached a conclusion, "The National Institutes of Health concludes that in both scenarios, that is whether the Bair Hugger is on or off, there is zero

1776

percent deposition on the patient for the contaminant sources and the heat generated by the patient provides some protection."
A. Correct.
Q. So zero percent being deposited on the patient?
A. Correct.
Q. And it says that the patient's heat provides some protection?
A. Correct.
Q. What does it mean that the patient's own heat provides protection?
A. So, if we could see air around in this room, we would actually see a plume of air rise by each of our bodies because we're warm and that's this hot air rises principle we talked about. The patient is warm. The patient is warmer than the room by quite a bit, and so the fact the patient is warm creates a plume of air, upward moving air by their skin and that upward movement of air protects the wound, and it sort of blocks any particulates from getting in.
Q. Well, to that point to the last sentence here, absolutely last sentence, "further if the operating room ventilation system is designed properly, contaminating particles from staff around the patient will not impinge on the surgical wound due to thermo plume dynamics."

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A. Correct.
Q. And is that what you were just describing?
A. Yes.
Q. Now, following on to this discussion of Memarzadeh, you were able to see the CFD that was put together by Dr. Elgobashi?
A. Yes.
Q. You saw it played for the jury?
A. Yes.
MR. BLACKWELL: Your Honor, we'd like to show that Elghobashi CFD again to point out a certain aspect of it.
THE COURT: All right.
MR. BLACKWELL: It's Plaintiff's 1491. Let's watch that again so.
(Whereupon, video played.)
Q. Now, Dr. Abraham, you have seen this Exhibit 1491, Dr. Elgobashi's CFD before?
A. Yes, yes.
Q. Did you see the original version of it?
A. I did.
Q. And by "original version, I mean the version that came from Dr. Apte?
A. Yep.
Q. Now you've seen the version that the jurors just saw?
A. Yes.

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Q. And this is the one they saw when Dr. Elgobashi was here?
A. Correct.
Q. Is the one that we just showed, was that the same version as the original one that you got?
A. I don't believe it was.
Q. And why don't you think that was the same one?
A. The one I saw was much slower, so you could actually follow the particles.
Q. In other words, this one was sped up?
A. Yes.
Q. Do you know for a fact it was sped up?
A. I do not know for a fact.
Q. All right. And if it was, do you know who did it?
A. I would not know that.
Q. And you wouldn't know why?
A. I would not not know why.
Q. But it appears to be modified in some way?
A. It appears to be sped up.
Q. So you did compare this that the jurors just saw, Plaintiff's 1491 with the original one, didn't you?
A. Yes, I did.
Q. And you relied on the actual video that Dr. Elgobashi did, true?
A. Yes.

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Q. Would being able to show the actual video to the jurors help you in explaining the difference between what they saw and in the original that you were seeing?
A. I believe it would.
MR. BLACKWELL: Your Honor, for demonstrative purposes, we would like to show Defense Exhibit 965.
THE COURT: You may.
MR. ASSAAD: No objection.
BY MR. BLACKWELL:
Q. So could we play 965, and let's look at this at the original speed.
(Whereupon video played.)
Q. It's a lot slower, isn't it?
A. It is a lot slower.
Q. You can stop it there, Brett. Thank you.
I want to have you look at this one more time. We'll look at it all the way through for purposes of seeing whether a single one of the particles in Dr. Elgobashi's CFD ever entered the wound. So would you look at that again and tell me if you ever see one particle into the wound?
A. I will.
(Whereupon video played.)
Q. So that's the same video at the original speed?
A. Yes.
Q. Now, did you, the ladies and gentlemen were able to see

1780

it as we all looked along, but did you see a single particle actually go into the knee area?
A. I did not.
Q. And did you hear a lot of testimony it only takes one?
A. I did.
Q. Did you even see one?
A. I did not.
Q. How does this relate to the concept of the thermo plume that you told us about and Dr. Memarzadeh spoke of?
A. Well, Dr. Memarzadeh wrote about this protective effect of the thermo plume because the patient's body is warm and the knee is warm, and so that creates a uplift of air, air is actually rising next to the knee and that prohibits or blocks particles from getting in.
Q. So the heat on the knee itself is protective?
A. Yes.
Q. And so what is the temperature coming from the knee and what temperature then was presumed as an input in Dr. Elgobashi's CFD?
A. The temperature of the knee is 37 degrees Celsius, about 98, 99 fahrenheit, and the temperature of the room is about 59 degrees Fahrenheit. So about a 40-degree difference.
MR. BLACKWELL: Thank you, Dr. Abraham. No further questions.
THE COURT: All right. Mr. Assaad.

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MR. ASSAAD: Thank you, Your Honor.
THE COURT: Mr. Blackwell, can I get a copy of those videos?
MR. BLACKWELL: Sure. Just call them.
MR. ASSAAD: Well, I'm asking --
MR. BLACKWELL: They're on the trial list.
CROSS EXAMINATION
BY MR. ASSAAD:
Q. Good afternoon, Dr. Abraham.
A. Good afternoon.
Q. We've met a few times, haven't we?
A. Yes.
Q. First thing I want to talk about is you said hot air rises all the time, correct? It never goes down, correct?
A. I don't know if I said that, but hot air does rise.
Q. Well, you said the one thing you disagree with Dr. Elgobashi are three things. You said he doesn't believe in hot air rises, that the jet -- his jet is too strong, and the -- that you believe all the air coming from the Bair Hugger comes out of the head and neck, correct?
A. I don't think I actually said any of those things. What I said was I don't think I said all the air comes out by the head or neck. I believe the air does come out by the head or neck. I believe it's the vast majority. I don't think I said all of it.

1782

With respect to jets, what I said was his jet kept a velocity for a very long distance, and I view the jets as spreading and slowing down.

And with respect to hot air rising, in my model the heat is always rising, and what I said was in his model underneath the table the heat goes down first and then it turns around and rises.

Q. And because in his model he has a drape over the arms, correct?

A. He has a drape over the arms.

Q. Okay. And I mean we live in Minnesota or you live in Minnesota, correct?

A. Yes.

Q. Okay. And I was just looking around up here, and I noticed that most of the diffusers are up high, correct? There's a diffuser there, there's a diffuser there, the hot air comes out of or the cold air. Correct?

A. Well, I would say this, that it appears that there are diffusers in the ceiling.

Q. Okay, diffusers in the ceiling. Are you saying when heat goes on to this room -- you're not saying that when heat goes on in this room that people that are fifteen feet below the ceiling never get warm. You're not saying that, are you?

A. No, I'm not saying that.

1783

Q. Okay. Now, with respect to the jet, you agree with me about the conservation of mass.

A. I agree mass must be conserved.

Q. So if you have a box that's a closed box with one entry and one exit, okay, whatever you put in one side the same amount is going to come on the other side with respect to mass, correct?

A. I agree.

Q. Okay. Now, I thought I heard you say that you calculated that the majority of the air comes out of the head and neck. Did I understand you correctly?

A. I did not say that.

Q. Okay. Because you didn't make any calculations with respect to whether or not the air, the majority of the air comes out of the head and neck in your model, correct?

A. Correct. The air coming out of the head or neck --

Q. Thank you. The next question I have is this. You've been saying or discussing a lot about how Dr. Elgobashi's model doesn't apply to operating room 4. Correct?

A. That is correct.

Q. And you've actually published something, a paper regarding your own model, correct?

A. Yes.

Q. And you said it was peer reviewed, correct?

A. Yes.

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Q. And you saw me object, correct?

A. Yes.

Q. We're going to get to that probably tomorrow, but I just want you know I haven't --

MR. BLACKWELL: Tomorrow is Saturday, Your Honor.

MR. ASSAAD: I'm sorry, Tuesday.

THE COURT: How much longer do you think you have with this witness?

MR. ASSAAD: Two hours, Your Honor.

THE COURT: Okay. Well, if that's even remotely close, we are going to not make it through this witness today. And it's a long weekend, so why don't we just stop now. The admonition that I gave you at the beginning about not talking, not reading anything, those all obviously continue to apply. And we will resume on Tuesday, the day after Memorial Day. Can you come back then?

THE WITNESS: Yes.

THE COURT: At 9:00 a.m. So we are in recess.

(Jury out at 4:11 p.m.)

(IN OPEN COURT)

THE COURT: All right. We're back in session here. You can be seated. I want to briefly let you know that the juror issue that we talked about before has not gone away. The juror wrote a letter saying she has -- she can't meet her bills, her employer is not even paying her.

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I made her stay all this week because I thought maybe she would change her mind or something would change. She just said no, it hasn't. She absolutely has to leave. And so I told her that she is excused.

MR. BLACKWELL: Yeah.

THE COURT: So that's.

MR. BLACKWELL: What else can you do?

THE COURT: I mean I could force her to stay but. I didn't. Pursuant to our earlier conversation about it, I just let her go.

I really thought maybe there -- I mean and I do believe that if there was any way she could stay, she would stay, but she's got bills to pay.

So enjoy your weekend, and we'll see you on Tuesday.

MR. ASSAAD: Your Honor, I'd just like to make a record real quick that on July 20, 2017, we sent a subpoena to Blackwell Burke on behalf of --

THE COURT: Okay. I don't have -- I just was in here for the purpose of the --

MR. ASSAAD: Could I ask a housekeeping matter? What's the schedule for next week? What's the schedule?

THE COURT: I think it's a regular week, as we discussed, with the exception of there's nothing on Monday and there is nothing on Thursday or Friday. I mean I

thought we -- did you have an additional question?

MR. ASSAAD: No, I just wanted to confirm.

THE COURT: Okay. Enjoy your weekend.

(Court adjourned at 4:14 p.m.)

C E R T I F I C A T E

I, Maria V. Weinbeck, and Renee A. Rogge, certify that the foregoing is a correct transcript from the record of proceedings in the above-entitled matter.

Certified by: /s/Maria V. Weinbeck
Maria V. Weinbeck, RMR-FCRR

Certified by: /s/Renee A. Rogge
Renee A. Rogge, RMR-CRR

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INDEX OF EXHIBITS

* * *

UNITED STATES DISTRICT COURT
DISTRICT OF MINNESOTA

Louis Gareis and Lillian Gareis,
Plaintiff,
v.
3M Company and Arizant Healthcare, Inc.,
Defendant.

VOLUME XI
File No. 16-CV-4187 (JNE/FLN)
May 30, 2018
Minneapolis, Minnesota
Courtroom 12W
10:08 a.m.

BEFORE THE HONORABLE JOAN N. ERICKSEN
UNITED STATES DISTRICT COURT JUDGE

(JURY TRIAL - VOLUME XI)

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Proceedings recorded by mechanical stenography; transcript produced by computer.

PROCEEDINGS

(10:08 a.m.)

(IN OPEN COURT)

THE COURT: Please be seated, everybody. I thought we would just very quickly go through a draft set of jury instructions so I can get a sense for the duration of discussion that might be necessary to hammer out any disagreements, so I'm really here to get my own sense for the scope of agreement or non.

What you have is not final and so don't look at the numbers at the top.

I did receive a proposed jury instruction from the defendants. Ms. Zimmerman, I assume the plaintiffs object to that?

MS. ZIMMERMAN: I'm actually not going to go through instructions. My -- counsel --

THE COURT: Who are you?

MS. O'LEARY: Good morning, Your Honor. My name is Leslie O'Leary. I'm here to argue jury instruction.

THE COURT: Who are you?

MS. O'LEARY: I'm a plaintiff's lawyer. I represent clients in the Bair Hugger litigation. I'm co-counsel with Rich Lewis who's also on the plaintiff's steering committee.

THE COURT: Have you been here during the trial?

MS. O'LEARY: Yes, I have, the entire trial.

THE COURT: What's your position with respect to proposed defendant's jury instruction No. 17?

MS. O'LEARY: Your Honor, we object to it.

THE COURT: All right. Your objection is sustained.

No. 1, members of the jury, as I told you at the beginning of the trial, I have not intended to suggest what I think your verdict should be. Corporations are entitled to the same -- somebody speak up if you have any problem as we go through here. Mere fact of an injury. When I instruct you, if you decide, I mean you have to meet a preponderance of the evidence. And then we go to the burden of proof. So I would take out that first paragraph because I just put that in, in the instruction before, the instruction before is some language. It's roughly O'Malley. And then the second two paragraphs of that burden of proof, fact has been proved by the preponderance of the evidence. In deciding what the facts are, you have to decide what testimony you believe. Recall what that evidence is. Expert witnesses. I'll give you a minute to read that.

Strict liability, cause of action.

Risk utility test.

Design defect, test for defectiveness.

Products liability proximate cause.

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MR. BLACKWELL: It's Defense Exhibit 953, 0001 and 0003; Defense 953, 0006 and 0008; Defense 953, 0012, 0014, 0017 and 0019; and then Defense 952, 0005. And I'll represent to plaintiff's counsel those are the same ones I used with Mr. Gareis.

MS. ZIMMERMAN: No objection, Your Honor.

THE COURT: All right. If they weren't previously received, they're received now.

MR. BLACKWELL: Thank you, Your Honor. We rest.

THE COURT: And with that, the defense rests. Ms. Zimmerman, for the plaintiff?

MS. ZIMMERMAN: Thank you, Your Honor. We have one additional housekeeping matter as well and then we would rest as well, in that we would offer Plaintiff's Exhibit 3002-0053. It's a medical record used in Dr. Presnal's deposition, and I understand it's without objection.

MR. HULSE: No objection, Your Honor.

THE COURT: All right. And that is received as well. So we have the plaintiff rests?

MS. ZIMMERMAN: Yes, we rest.

THE COURT: All right. So members of the jury, you've now heard all the evidence. What remains is for you to hear the arguments of the lawyers and my final instructions. As you may imagine, I have to go over a few

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things with the lawyers, so I'm going to send you to lunch now and then when you come back, we'll give you the closing arguments and the final instructions and you can begin your deliberations.

Once you begin your deliberations, you will be in charge of your schedule. So I know that we said, and we're not planning, we wouldn't have court tomorrow or the next day, but in terms of your own deliberations, it may be that you have a verdict today, it may be that you want to come back, but that's something that will be in your hands.

And once a jury is deliberating, all I ask is that you let me know when you decide what your hours will be so that I can make sure that I've got court security people around, but in the meantime, you will be at lunch. And so we'll start with the closing arguments of the lawyers, and the order is that the defense goes first and the plaintiff, having the burden of proof, goes last, and then you get the instructions. So that's my message for the moment. We're in recess. 12:30.

(11:34 a.m.)

(Lunch recess until 12:30)

(12:47 p.m.)

THE COURT: Please be seated. And but let's have a volunteer to close the door. I'm looking at you,

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volunteer. Thank you very much.

Are the defendants ready to proceed with closing?

MR. BLACKWELL: Yes, Your Honor.

THE COURT: Mr. Blackwell, you may proceed.

MR. BLACKWELL: Thank you, Your Honor.

CLOSING ARGUMENTS BY MR. BLACKWELL

MR. BLACKWELL: Good afternoon, ladies and gentlemen of the jury. This is it. We've come down the home stretch. All of our efforts and work and anxieties around trying to find the best way to present our case to you so that you would understand the case is coming to a close and whatever stress anxiety I felt will soon be transferring to you as the ladies and gentlemen of the jury.

And we heard from a number of witnesses that took the stand there and testified to you all, and every single one of them started holding up their hands and taking that oath that they would tell you the truth, the whole truth, and nothing but the truth. And that matters because what you're going to reach in this case is called a verdict. A verdict is a Latin word that means the truth. Now, you think that's an easy thing. You listen to the facts. You call it as you see it, but it's not always so easy because when it comes to their levels of truth and telling the truth, you have to be able to tell the truth in season, that

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is, when it's an easy truth to tell, but you also have to be willing to tell that truth when it's out of season, that is, when it's a hard truth. In a case like this, where you have a real family, real people, who love each other, and you have to look at the facts and say if the burden of proof wasn't met, you didn't meet your burden of proof. Hard truth.

One of the hard truths about this case that you know and have learned by now, this is not a case that started with an orthopedic surgeon, a treating doctor, who said to the patient you have an infection in your hip from the surgery and it was caused by a Bair Hugger. That's not how this case started. This case didn't start with persons who were looking for lawyers. This started with Mr. Gareis sitting at his house watching television when an ad came on with lawyers looking for clients.

And what did this translate into? We talk about truth and seeking truth. One of the first things you saw starting in opening statement was this, ladies and gentlemen: truth. On the left you'll see the CFD from the plaintiff that they showed you in opening statement. If you can go ahead and play it, Brett.

And so what you see on the left, all kind of particles that start to rain down like a blizzard in a matter of seconds. The truth that you learned in this case

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-- just one moment. The truth that you learned in this case is that the video that you saw on the left had been manipulated. It's already an animation, but it was sped up. You weren't told it was sped up. It wasn't acknowledged that it was sped up until such time as we told you because speeding up has the particles fall like snow when the claim is that this particles spewing everywhere. Speeding it up makes it hard for you to see the truth that you learned when we showed you the original at real sped and you could see that even in this animation that these lawyers brought to you, not a single particle ever fell in the wound. Harder to see when it's sped up. And why is that? It's because of something called a thermal plum. The heat is given off by the body, has its own buoyance that caused the particles to rise, and not a single particle, even in the animation that plaintiffs brought, ever, ever fell in the wound.

Now, the words at the top will say for your convenience, and the reason that that's there is because the explanation given yesterday in exchanges for the witnesses, this was done for your convenience, for you, the jurors. What you're entitled to have always is, to the extent we can give it, is the straight truth. And if you've ever had the experience in your life of having something that you used to own, you don't know what happened to it, but then you see it on the shelf of somebody you know, on the wrist of somebody

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you know, and you call them on it, and they said something like, I was just taking care of this for you, this was done for your convenience, do you believe them? And why would you?

Always pays, as your parents always say, all you had to do was ask, all they had to do was let you know. We showed you a time lapse video too. We told you that it was a time lapse video, not that that was somehow the real surgery.

So when we talk about burden of proof, it's a burden of doing the best you can to bring about the truth. Don't put up a picture that gives a distorted image of a reality and not even tell you right up front in the opening statement. But I can't even stop there. Because the other thing, and you might remember two minute from the time I said hello to you in opening statement, I said to you that I hope the very first thing they do is to turn on that Bair Hugger and let you come up here and experience it for yourself and see what you think. I said that for a reason. It's because I knew what was going to be said and because I knew that if you experienced it for yourself, if a picture is worth a thousand words, then one experience is worth a thousand pictures and you would hear testimony from people saying things like the Bair Hugger was blowing drapes around. You heard that from Dr. Stonnington. You

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experienced that in one second and realized you could barely feel anything, even inches away from the Bair Hugger, much less blowing big drapes around. Couldn't have been true. Let you experience it for yourself, and the last thing they would do is plug in the that Bair Hugger and invite you to come down and see for yourself. Burden of proof truth.

I want to review some of the evidence with you in terms of what you've heard and what you have seen about the Bair Hugger, how well it works, its efficacy, and let you answer the question, as you listen to the evidence, have they shown you? They've shown you one alternative product, this Tablegard. Ask yourself the questions, have they ever shown you that the Tablegard would even work as well as the Bair Hugger? Have they ever shown you that whatever criticisms they have of the Bair Hugger, has there been any testing that would prove to you that you wouldn't have exactly the same concerns these lawyers would, with respect to the Tablegard, had they ever tested it and brought you the result? Have they shown you anything?

Now, what I told you in opening statements I come back to here in the closing statement. I told you then that no scientific study has ever concluded that the Bair Hugger system causes surgical infections. You've been here for weeks. And think about all the studies you've heard. You've heard talks about particles. You've heard talks

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about bubbles. Nobody has ever been infected by a bubble. Nobody has ever been infected by a particle. You've never said that in your life.

And if particles cause infections, then why can't you ever find a single study that made an association between the Bair Hugger and surgical infections or even showed that the Bair Hugger increased bacteria at the surgical site? If it's increasing particles and it's on the particles, where is the proof? Burden of proof. It's not a burden of accusation. It's not a burden of saying things. It's not a burden of prejudgment. It's a burden of proof. Why isn't there a single study? And when I told you that the Bair Hugger was the most tested forced air warming device in the history of this country, if not the planet earth, they may have ridiculed me but they didn't come and tell you that one was more tested, did they? Test after test, test after test, test after test, and not a single test concludes that the Bair Hugger either causes infections or increases bacteria other surgical the site no matter how many particles they want to talk about or bubbles, bacteria is what causes infection.

And I told you that the majority of surgical site infections come from bacteria in the patient's own body. And I'm going to come back to that again in reviewing the evidence with you to show you what you've heard in that

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THE COURT: Hold on. Stop. Please stop it. Stop it. Thank you.
MR. FARRAR: Sorry, I'm not good on Macs.
MR. BLACKWELL: This was never put in evidence, Your Honor.
THE COURT: Is this in evidence?
MR. BLACKWELL: No.
MR. FARRAR: He just showed it.
THE COURT: Mr. -- I'm asking if this has been received in evidence.
MR. FARRAR: I do not believe so, Your Honor. I don't think it's admitted. It's a demonstrative.
THE COURT: Okay. Don't play it then.
MR. FARRAR: We brought you Dr. Elghobashi. Some interesting things were said about Dr. Elghobashi and CFD, that you can't trust it. He told you that he built Star Wars with it in the 80's. He builds aircraft carriers. He does surgeries on people's throats using it to determine airflow to where that surgery has to be. That's reliable stuff. That's cutting edge.
There was criticism about Dr. Elghobashi that, well, the video was sped up. He told you these videos are 45 seconds and he's playing it for five. There's no deceit in that. He's telling you exactly what he's doing. He ran it on a supercomputer for 200 -- I'm sorry, 2 million hours,

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2 million computing hours, to come up with the results. He tracked ten micron particles, and the question he to ask was -- or answer, does the Bair Hugger cause ten micron particles to reach the sterile field? And he answered yes. It absolutely does. There's criticism that none of the particles go right in his knee. It's a 45-second video, not a two-hour surgery, but they're there. When they're right around the sterile field, what happens when you take the prosthesis, the device, and put it in him? You're going right through the particles, right through the bacteria. His study was published, 2017. We talk about what does everybody else have? What information does everybody else have? You have the most. You saw the study.
This is the OR, with the squames on the bottom, and it's 3 million ten-micron squames, big enough to carry bacteria.
(Whereupon video played.)
MR. FARRAR: And what did it do? It rose over the surgical site. When you test something like a Bair Hugger, when you're making a test, you want everything constant. You want the only thing to change is the one thing you're testing, the Bair Hugger. 3M says, well, look, there's no people moving. You can't replicate people moving. People would move differently every time. There's no doors opening and closing. You can't replicate doors opening and closing

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every time. You keep everything constant and you see what the one thing you're studying, what effect it has on the environment. It's exactly what Dr. Elghobashi did. He ran it on a supercomputer.
And you heard from Dr. Abraham. Dr. Abraham did 40 days on his home computer and this is what he got, some sort of error, error messages. He just hit delete and kept moving. Dr. Abraham devotes his life work, if you listen to him, to computational fluid dynamics and he testified it's always wrong. He also testified he always gets error messages. He published his article through a friend of his, not the peer reviewed double-blind process, somebody he know and works with called and had it published.
He assumed -- he assumed that all the heat comes out of the neck and head of the Bair Hugger, so a patient laying with his arms to the side, the Bair Hugger strapped all the way down, with all the drapes, he told you those drapes, air can't get through those drapes. They are impenetrable.
When you turn it on and blow air on people, blow hot air on people, he says none of that goes down. Does that make any sense? There are drapes there holding the air in. When you keep putting more air in, the air in there has to go somewhere. It can't just stay. You can't just keep putting air in the spot. So it's going to the path of least

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resistance. It's going to go right underneath those drapes, still warm, and it's going to come right back up the other side. And when it does that, it's carrying particles. It's carrying bacteria. He assumed it all came out of the head and neck.
He also didn't answer the question we're here to answer. Where do the particles go? He told you particles do not follow streamlines and he modelled streamlines. Where do the particles go? Where the streamlines go is not relevant to what decisions you have to make. Ultimately, you have to ask, look back at your notes and ask yourself, why do they call Dr. Abraham? He's always wrong, sometimes helpful, didn't study when we're supposed to be studying. He testified point blank I'm not an expert in any of the literature. He wasn't helpful to that -- for you they read some through them, just as a mouth piece, but it wasn't useful. Look back through your notes and figure out why was he here?
I think the evidence is abundantly clear that the Bair Hugger causes infections. That's a thing. We have the evidence from the puzzle like Dr. Jarvis put together for us. We have the evidence from Dr. Borak talking about being a puzzle. We have the McGovern study. That's the real world study showing association. And then we have Dr. Elghobashi's work proving it on computational fluid

EXHIBIT DX14

TO DECLARATION OF BENJAMIN W. HULSE IN SUPPORT OF DEFENDANTS' MOTION FOR RECONSIDERATION OF THE COURT'S DECEMBER 13, 2017 ORDER ON GENERAL CAUSATION

UNITED STATES DISTRICT COURT

DISTRICT OF MINNESOTA

Louis Gareis and Lillian Gareis, Plaintiff, v. 3M Company and Arizant Healthcare, Inc., Defendant.	File No. 16-CV-4187 (JNE/FLN) April 12, 2018 Minneapolis, Minnesota Courtroom 12W 9:38 a.m.

BEFORE THE HONORABLE JOAN N. ERICKSEN
UNITED STATES DISTRICT COURT JUDGE

(DEFENDANTS' MOTION FOR SUMMARY JUDGMENT, MOTION TO EXCLUDE EXPERT TESTIMONY AND OPINIONS OF DRS. STONNINGTON AND JARVIS, AND MOTION TO EXCLUDE EXPERT TESTIMONY OF SAID ELGOBASHI, PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT)

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But both Dr. Elgobashi and Dr. Abraham used the same reduced volumetric flow rate for the 505 machine, and that changed from 44 cubic feet per minute to 30 cubic feet per minute. And, again, both experts and CFD used the same numbers there. And really at the end of the day, it's a less powerful hair dryer or shop vac. But at the end of the day, they have the same impact in an operating room.

So because Rule 702 would allow Dr. Elgobashi's testimony because he uses reliable methodology, and because it is relevant to the issues that will be presented to the jury in this matter, we think that Defendant's motion should be denied. And to the extent the Court has questions, I'm happy to entertain those.

THE COURT: There are pictures, diagrams, you know, those three-dimensional cube things that Dr. Elgobashi uses. And I'm thinking about the ones where he's got the pictures of the squames not reaching -- he's got them, you know, down below the operation table when the Bair Hugger is off. And then you turn it on, and they come up to the patient.

MS. ZIMMERMAN: They do.

THE COURT: So it strikes me that there might be a difference between the utility of his opinion and the potential prejudice of a picture that shows that no squames are getting up above the operating table in a

counter-factual operating room. Like I think, okay, the -- I'm going to call it it's not a simulation but, you know, his --

MS. ZIMMERMAN: The CFD.

THE COURT: His thing, when the blower is on seems like one thing to me, and I think, okay, fine, that can come in. But for the jury to see this diagram of what happens when it's off, well, that's not what happens or that is not a picture of what would happen if the Bair Hugger were in the off position in Gareis's operating room.

I guess my question is do you see a difference between the Elgobashi opinion with the Bair Hugger I guess to put it simply in the off position as opposed to the on position?

MS. ZIMMERMAN: No, Your Honor. And videos were produced pursuant to the CFD for both on and off, and the kind of images that I think Your Honor is referring to are reasonably essentially a still-frame shot of the videos that have been done. And so the same could be done with the machine off, for example, which shows in the CFD modelling when the Bair Hugger is off, that none of the squames reach the operating table.

THE COURT: Yeah, I just think it's different because when it's on, you want to be able to show that that can stir up the squames, and it shows that.

MS. ZIMMERMAN: Yes.

THE COURT: And you're using that as a general scientific, like this is a scientific thing --

MS. ZIMMERMAN: Yes.

THE COURT: -- and you can watch it happen.

MS. ZIMMERMAN: Right.

THE COURT: But to say it's an actual scientific thing that the squames don't reach the operating table unless you turn this on, that's a slightly, that's a different opinion.

MS. ZIMMERMAN: Well, I think, Your Honor, that that really goes to exactly why this is a scientific study that Dr. Elgobashi did. So what he did was he had a room, and he plugged into the computer. And I appreciate this is an over-simplification of what he did, but the CFD analyzed given the air that's coming into the room, what is the impact on the same number of squames placed in the same places on the floor?

And then he changes one thing, he adds the Bair Hugger and turns it on so that he can see what if any impact does the Bair Hugger have on this model operating room? Which is precisely what 3M has done with the CFDs that they have done prior to this litigation and then, you know, during the course of this litigation with respect to Dr. Abraham was to understand --

THE COURT: Right, right. But as applied to the plaintiffs' case that the Bair Hugger is what caused Mr. Gareis's infection, to say, look, here's what would have happened if the or to do a demonstration that could reasonably be taken by the jury as a demonstration of what would happen had the Bair Hugger not been there, no squames get to the injury, first, let's turn it on, and they do. There's a prejudice there that's not there if the scientific principle of the contribution of the Bair Hugger to air movement is placed before the jury because then, you know, well, okay, here's what the movement could be, it depends, you know, here's what we put in here. But, of course, it could be this, it could be that, but the scientific idea that the Bair Hugger can cause a stir-up remains. But it's a different point to say no Bair Hugger squames stay below four feet or whatever it is, or three feet, and with it they go above it.

I can't get myself over the notion that there's a difference in those two opinions and that once we're talking about it getting above the operating table, and the issue is did the Bair Hugger contribute or cause squames to get above the operating table in Gareis's case? And then you've got this diagram of squames staying in a safe location in the absence of a Bair Hugger, it's pretty hard to explain to a jury that that's not meant to demonstrate that this is what

happened in Gareis's case.

There's a little bit of the same problem with the stirring it up, but that's a scientific principle that doesn't have to be so tied to the facts of the particular case. I guess that's what I'm struggling with, and I don't know if that constitutes a question or if you want to talk about that.

MS. ZIMMERMAN: I would certainly like to assist the Court with that. I think that to the extent, so the CFD whether done by Dr. Elgobashi or Dr. Abraham or, you know, Olmsted and Memarzadeh that did this before we got to this courtroom, none of it would be helpful to anyone unless it was comparing it to something else. So you have to have a point of comparison to understand, well, does this matter or not?

THE COURT: Yeah.

MS. ZIMMERMAN: If it was just the Bair Hugger on, then we would know, well, that happens but is it because of the Bair Hugger or is that because there's just this stuff blowing around all the time.

THE COURT: Right.

MS. ZIMMERMAN: And so that was, I guess, the idea and the reason that Dr. Elgobashi did it once without the machine on and then again with the machine turned on, and we certainly think that those are critical to understand the,

you know, the impact of this particular device on a general operating room.

THE COURT: Right. Well, that's the struggle because, of course, to show that in the on position that has some effect, you want to show something about, well, here it is --

MS. ZIMMERMAN: What's it look like off.

THE COURT: But he makes a point of there being a level below which the squames don't travel in the off position but they do, and it's a relevant level. And that relevant, that level, is it necessary to demonstrate the basic principle that he's trying to show that he, that the jury see a picture of or have him testify about that particular level?

MS. ZIMMERMAN: Well, I think, Your Honor, that Dr. Elgobashi has been posed some questions about this, and I think his answer to that question would be it only gets worse, that, you know, to the extent that the squames are coming off of a person and so they start at shoulder level rather than close to the floor, that the assumptions that he did and that his CFD calculates really assumed kind of the worst case scenario because it is harder for squames that are already near the floor to travel up and get to the surgical site.

THE COURT: But that's not shown in his CFD.

MS. ZIMMERMAN: That's correct, that's correct. And I think that that's certainly something that I expect will be part of the cross-examination that is posed to Dr. Elgobashi as he tries to explain to the jury what general scientific principles show about the impact of the Bair Hugger on an operating room. But the only way for him to be able to demonstrate and explain to a jury what the impact is of this machine on an operating room is to also have modelled what happens in an operating room with the same squames put in the same exact places without a Bair Hugger --

THE COURT: He doesn't have to talk about a specific, there's just -- why did he run it, well, I guess I mean I know the answer to that, it's a rhetorical question. Why did he run it with the squames staying below a certain level and then when you turn it on, they go above a certain level? Well, obviously, it's because he's trying to show that the Bair Hugger makes the squames go above the relevant point.

MS. ZIMMERMAN: So I think what Dr. Elgobashi would tell you or would testify is that these squames are placed very close to the ground, and the intent was to see what happens if anything when the Bair Hugger is turned on. When we approached him, and he's testified about this during deposition, he told us that he was going to publish the

results of this study whether they were favorable to plaintiffs or whether they were not because this was an interesting scientific question.

THE COURT: Yeah, it's not a -- that's not my question. The question I guess has to do with the prejudice of him talking about what would happen in Gareis's operating room if the Bair Hugger had not been in the on position?

MS. ZIMMERMAN: Okay, well, he --

THE COURT: He's not going to say this is what happened in Gareis's, is what you're going to say.

MS. ZIMMERMAN: That's correct.

THE COURT: Okay. Mr. Goss, do you have anything to say about that or anything? Because, Ms. Zimmerman, you're about --

MS. ZIMMERMAN: I think I'm done with this one, but I'll wait to see if there's something else I need to add here.

THE COURT: Okay.

MR. GOSS: All right. Just a couple of things, Your Honor. I wanted to come back to the *McKnight* case, and the testing that the Eighth Circuit said should not have been admitted in that case was not actually intended to be an exact replication of the accident. And I'll show you what it says. So it says, "*McKnight*, the plaintiff, specifically stated that the experiment's test results are

not intended to serve as a reenactment of the explosion."

THE COURT: Yeah, right. Okay, fine, you know, whatever.

MR. GOSS: Okay.

THE COURT: I'm not going to keep Elgobashi's scientific CFD. I'm going to keep it out all together.

MR. GOSS: Okay.

THE COURT: I am concerned about undue prejudice from representations in his work about the off state squame distribution. Is there anything that could be done in your imagination to limit that prejudice while still allowing the testimony about the fundamental scientific principle that's demonstrated by his computer modelling?

MR. GOSS: Well, Your Honor, the squames blow around everywhere in the off state too. So it's not like they're just staying on the floor. And if you look at the videos, you know, you see maybe a little more activity with the on than the off, but everything is traveling up even with the Bair Hugger off.

So the key question is how do you get to that difference just by turning on the Bair Hugger, and there are so many things that aren't included in that model that could do the same thing. And the Bair Hugger being in the off state having the squames rise shows that all sorts of things can influence the movement of squames, movement of people,

EXHIBIT DX15

TO DECLARATION OF BENJAMIN W. HULSE IN SUPPORT OF DEFENDANTS' MOTION FOR RECONSIDERATION OF THE COURT'S DECEMBER 13, 2017 ORDER ON GENERAL CAUSATION

UNITED STATES DISTRICT COURT
DISTRICT OF MINNESOTA

In Re: Bair Hugger Forced Air Warming Devices Products Liability Litigation	File No. 15-MD-2666 (JNE/FLN)
	October 25, 2017
	Minneapolis, Minnesota
	Courtroom 12W
	9:07 a.m.

BEFORE THE HONORABLE JOAN N. ERICKSEN
UNITED STATES DISTRICT COURT JUDGE

THE HONORABLE FRANKLIN L. NOEL
UNITED STATES MAGISTRATE JUDGE

THE HONORABLE WILLIAM H. LEARY
RAMSEY COUNTY DISTRICT COURT JUDGE

(MOTIONS HEARING - VOLUME II)

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PROCEEDINGS

(9:07 a.m.)

THE COURT: Please be seated. Mr. Sacchet, we cut you off yesterday. Did you have any last thoughts that you wanted to clear up?

MR. SACCHET: There is one thought I did want to clear up.

THE COURT: Yeah. I'd be happy to hear from you. If I had a heart and if I had feelings, I would have felt bad for cutting you off.

MR. SACCHET: Don't worry. I guess I should clarify your question, though, Your Honor. With respect to the time, are you just referring to Holford's motion or Borak's motion as well?

THE COURT: I think we're almost done with Holford.

MR. SACCHET: Yeah. I agree.

THE COURT: What I was wondering is if you had a couple of things you wanted to say about Borak, and I know that Borak is very dependent on Holford, and that comes through, of course, in your memo. So I don't anticipate that you have too much to say, and if you want a specific number of minutes, I can make up a number.

MR. SACCHET: I was hoping maybe to go 10 minutes on Borak.

THE COURT: All right.

MR. SACCHET: Unless that's extreme.

THE COURT: No. Do it.

MR. SACCHET: Okay. And I did have a housekeeping matter. I have copies of the decs that we presented yesterday that we would be happy to give the Court. I conferred with my friends on the other side, and they have copies as well.

THE COURT: No one is admitting to being your friend.

MR. SACCHET: I would hope they would.

THE COURT: So, Mr. Blackwell, do you have a similar dec?

MR. BLACKWELL: We do, Your Honor.

THE COURT: Okay. Would you mind just giving us those a little bit later because we're over -- under whelmed with space up here.

MR. SACCHET: I understand. The only matter left with respect to Mr. Albrecht and the under power calculation that was brought up at the end of my presentation yesterday and --

THE COURT: Albrecht?

MR. SACCHET: Mr. Albrecht opines on the same matter that Professor Holford did with respect to the double power calculation. I wanted to read a quick excerpt from

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Mr. Albrechts' testimony. Mr. Albrecht's testimony has been cited often and I think miscited as well, and when he was asked specifically about what happens when you control for both hypothetical confounders, does it actually in fact reduce the odds ratio or make it disappear.

And yesterday I explained to the Court that when you cut the population of the McGovern study in half from approximately 2400 patients --

THE COURT: Down to 600, you don't have a statistical significance.

MR. SACCHET: There's an issue of numbers, and when Mr. Albrecht was asked this question: If you were to analyze the data factor taking into consideration the antibiotics and the Rivaroxaban and if that factor goes out, do you still thing there would, even with observational data, it would show a difference between Bair Hugger and HotDog.

And Mr. Albrecht responded, I don't know. There's a period of time here which comes into play. There's possibly not enough infections, infections to do a multi varied analysis like that where it's properly powered. I'm not so sure we'd be able to tease out the effect of multiple factors at the same time with the data set that has, you know, few infections like that over multiple cuts of variables.

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So that's Mr. Albrecht's testimony as to the issues with controlling for two hypothetical confounders on an extremely small duty set within an extremely reduced infection risk ratio.

MAGISTRATE JUDGE NOEL: On that point, authors reaffirming their conclusions in McGovern, is there some place in your memo, I think there is, but I don't have it clearly in mind, and if not, is there somewhere where you can direct us to where each of the authors who were deposed reaffirmed the conclusion of the study?

MR. SACCHET: I can.

THE COURT: And that conclusion being that there's an association?

MR. SACCHET: I can. If you can give me a minute, though, and this could take an unnecessary amount of time.

MAGISTRATE JUDGE NOEL: If you don't want to take the time right now, if one of your colleagues can be looking for that, and you can give it to us at some point before you're done.

MR. SACCHET: I appreciate that. Okay.

THE COURT: Would it be in your memorandum in support of Professor Holford?

MR. SACCHET: So I believe we cited it in two memos. I believe I did direct citations in the opposition to 3M's motion to exclude Samet with testimony from

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Dr. McGovern saying that he stands by the 3.0 risk ratio not only based on the published McGovern study, but also based on the data that was collected after the study. That statement is in our papers.

Also, in our Holford papers we cited deposition testimony from both Dr. McGovern and Professor Nachtsheim to the same effect, although I don't believe we included a parenthetical citation stating the precise words of their testimony, but I will look for that, and we will present it to the Court in due time.

On to Dr. Borak, you are very correct, Your Honor, that Borak's report in large part relies on Professor Holford's analysis, so I will not be repeating that. What I will do is identify the three ways in which Dr. Borak's testimony differs from Professor Holford's, and I will go through that very quickly.

The first is that with respect to Dr. Borak's opinions regarding the relationship between SSI measures and the outcome of interest in this litigation, deep joint infection, he proffers additional testimony on that subject matter, precisely identifying two particular SSI measures that Professor Holford failed to identify. Those are namely, one, the impact or potential impact of skin preparation; and two, the potential impact of NSSA's nasal screening, and he analyzes those in his report.

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The first thing to bear mentioning again is that Dr. Borak admitted on the record that he did in fact conflate in his report SSI with DJI, and as I was saying yesterday, they have different etiologies, and I won't re-explain that for the Court again in light of the time, but with respect to the two particular factors of interest that he did analyze, the first was skin preparation.

And just as a quick background, some of the patients in the McGovern -- in the Bair Hugger arm received a solution called Povidone-iodine, and that changed in the HotDog group where some patients received chlorhexidine, and Dr. Borak speculates, and it's apparent in the record, that that change, even though it deals with topical skin preparation, could have impacted DJI.

And in this colloquy, he makes that clear, and I won't reread it because it's here in the record, and we will provide copies for the Court, but the notable statement is at the end where he essentially says, to the extent that this would have an impact on DJI, then it would be considered a confounder, but he never concludes that skin preparation is in fact a confounder.

MAGISTRATE JUDGE NOEL: Is there any studies post McGovern like the one you were describing on the word I can't pronounce.

MR. SACCHET: Rivaroxaban?

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MAGISTRATE JUDGE NOEL: Yes. That's the one where there was a post study that shows that it doesn't confound. Is there any post McGovern study on either the skin preparation or the antibiotic change or any of the other alleged confounders, or is it just that -- the one I can't?

MR. SACCHET: Rivaroxaban. I'm not particularly aware of studies with respect to skin preparation and MSSA nasal screening that has concluded that there is a relationship, and to be honest I think it would be a curious conclusion because when I deposed Dr. McGovern and I asked the question, Are you aware of any studies that would evaluate this relationship, he was surprised that I would even ask that question because skin preparation is a topical on your skin. There is no relation to the joint.

The MSSA nasal screening is in the nose. It can perhaps cleanse bacteria, but the biological plausibility is questionable, and in light of that, I don't think the authors have taken the step to conduct a true study to show that it is not a confounder, but it's the opposite burden. In order to show that it is a confounder, both the citations in Dr. Holford and Dr. Borak's report show that there must be literature showing a substantial difference between one regimen and another, and based on that literature, you can conclude that there is confounding.

You cannot conclude that there is confounding

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based on an a priori assumption in the absence of evidence that there is confounding. You need scientific proof to make that determination.

MAGISTRATE JUDGE NOEL: But how is -- everybody gets hoisted by their own by tar. Isn't that the point they're making about your evidence on bacteria generally? In other words, your point is, got to be some way to get that bacteria in there. Common sense suggested if you're sucking up dirt from the floor and blowing it up the other end, maybe it's going to be a source of the bacteria that gets into the joint.

But they keep saying you have no evidence of that. You have no measured study showing increase in bacteria on the agar plates or however else you can count bacteria. So isn't that -- am I missing something?

MR. SACCHET: I'll address it two ways. First, there are studies showing statistically significant increases in bacteria as a result of the Bair Hugger, and that is the Moretti study.

MAGISTRATE JUDGE NOEL: Okay. I'll have to look at Moretti again because Moretti has come up, but Blackwell comes back and yells at us that no, Moretti doesn't say that.

MR. SACCHET: Review that. So I can tell you that although there was a statistically significant increase in

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bacteria as a result of the Bair Hugger, there were no deep joint infections, but that's because there was 20 patients. Again, you're not going to have statistically significant increase in infection when your population is 20 persons.

So they want to come up here and argue that that study doesn't matter because of that. In my view, it's scientific sophistry. What it does show in its plain text is that there's a statistically significant increase in bacteria when the Bair Hugger is turned on, and that's fact. My second response would be, well --

JUDGE LEARY: I'm going to get back to when you make a comment like, in my opinion it's sophistry. I keep on wanting to get back to the idea of, you have to establish, plaintiffs have to establish, and the defendants as well, for any proposition they're asserting with regard to scientific principle that it's in the record, and the flavor of comments within my opinion, it really doesn't advance the ball.

MR. SACCHET: There is a document that we've put in the record, Your Honor. It was cited in our response to 3M's motion to exclude Dr. Samet, Dr. Jarvis and Dr. Stonnington in which 3M's corporate witness Mr. Al van Duren explains that in order to have a properly powered study, there would need to be more than a thousand patients, and he determined that that was not a good study to conduct

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because it would have been a bad career move.

JUDGE LEARY: So does he support your opinion that the other topic that you're addressing was sophistry? I mean, he makes that statement as a matter of principle, but as applied to the statement you made, does he express any opinion?

MR. SACCHET: He does not directly say that Moretti was under powered with respect to deep joint infection rates, but he does say you need at least a thousand people or more.

JUDGE LEARY: I understand that.

THE COURT: So the question that keeps bothering me, I may or may not be able to articulate it. In making a distinction between DJI and SSI, the plaintiffs make the what appear to be valid scientific points about the differences, and yet in the theory of how Bair Hugger increases DJI, you look at information about bacterial counts on the surface of things, like agar plates or bubbles or -- these are, you're counting things that are above the surface, not down below.

And at several points, it seems that you're arguing that nothing that happens on the surface, nothing about SSI, has any relevance at all to the question of the ability of any instrumentality that increases air flow or bacteria in the air, that the SSI has no bearing whatsoever,